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Scientific and Technical Information Center

SEARCH REQUEST FORM

Date: 4/27/01 Requester's Full Name: Grace Hsu Examiner #: 77391

Art Unit: 1627 Phone (30 6) 7005 Serial Number: 09/148,973

Results Format Preferred (circle): PAPER DISK E-MAIL

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Method of Administering An AMPA Receptor Antagonist

Inventors (please provide full names): Lee Whittemore

Earliest Priority Date: 9/4/98

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known.

For Sequence Searches Only *Please include all pertinent information (parent, grandchild, divisional, or issued patent numbers) along with the appropriate serial number.*

Please Search Claims 1-9

(2) Les p 4 For AMPA receptor Antagonists

09/148973

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✓ Structure (#)

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_____ Litigation

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✓ STN _____ Dialog

_____ Questel/Orbit _____ Dr.Link

_____ Lexis/Nexis _____ Westlaw

_____ WWW/Internet

_____ In-house sequence systems (list)

_____ Other (specify)

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     (FILE 'HOME' ENTERED AT 16:10:22 ON 30 APR 2001)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 16:10:35 ON 30 APR 2001
               E GREENAMYRE J/AU
L1           80 S E4-E10
               E CHENARD B/AU
L2           73 S E4-E9
               E WELCH W/AU
L3           15 S E3,E14
L4           73 S E20-E25
               E MENNITI F/AU
L5           38 S E4-E7
L6          252 S L1-L5
L7           22 S L6 AND AMPA
L8           10 S L6 AND AMINO(L)HYDROXY(L)METHYL(L)ISOXAZOL?

     FILE 'REGISTRY' ENTERED AT 16:14:04 ON 30 APR 2001
L9            1 S 77521-29-0

     FILE 'HCAPLUS' ENTERED AT 16:14:10 ON 30 APR 2001
L10        1054 S L9
L11           2 S L6 AND L10
L12          24 S L7,L8,L11
L13           1 S L6 AND DIETHYLAMINOMETHYLPYRIDIN? (L) QUINAZOL?

     FILE 'REGISTRY' ENTERED AT 16:16:00 ON 30 APR 2001
L14           1 S 59-92-7
               E D-TYROSINE, 3-HYDROXY-/CN
L15           1 S E3
               E DL-TYROSINE, 3-HYDROXY-/CN
L16           1 S E3
L17           1 S 28860-95-9
               E C10H14N2O4/MF
L18           5 S E3 AND BENZENEPROPANOIC AND HYDRAZIN?
L19           3 S L18 NOT (ESTER OR 5 DIHYDROXY)
L20           1 S 322-35-0
               E C10H15N3O5/MF
L21           5 S E3 AND 46.150.18/RID AND SERINE AND TRIHYDROXYPHENYL
L22           5 S L21 AND HYDRAZ?
L23           4 S L22 NOT 5
L24           3 S L23 NOT 4228-70-0
L25           1 S 199655-81-7
L26           1 S 199655-81-7/CRN

     FILE 'HCAOLD' ENTERED AT 16:21:33 ON 30 APR 2001
L27           0 S L25 OR L26

     FILE 'HCAPLUS' ENTERED AT 16:21:37 ON 30 APR 2001
L28           4 S L25 OR L26
L29           4 S L28 AND L6
L30           1 S L28 AND L10
L31           4 S L28 AND AMPA
L32           4 S L28-L31

     FILE 'REGISTRY' ENTERED AT 16:23:03 ON 30 APR 2001
L33           3 S L14-L16
               SEL RN
L34          95 S E1-E3/CRN
L35           3 S L17,L19
               SEL RN
L36          22 S E4-E6/CRN
L37           3 S L20,L24
               SEL RN
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Point of Contact:
Jan Delaval
Librarian-Physical Sciences
CM1 1E01 Tel: 308-4498

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L38           8 S E7-E9/CRN
L39           7 S L34 AND L36,L38
L40           2 S L39 AND 2/NC
L41           7 S L38 NOT L40

     FILE 'HCAPLUS' ENTERED AT 16:24:25 ON 30 APR 2001
L42         102 S L40
L43        9797 S L33
L44       14549 S DOPA OR LEVODOPA
L45       15989 S L43,L44
L46         843 S L35 OR L37
L47        1209 S BENSERAZIDE OR CARBIDOPA
L48        1496 S L46,L47
L49        1085 S L45 AND L48
L50        1127 S L42,L49
L51           3 S L50 AND L10
L52           6 S L50 AND AMPA
L53           0 S L50 AND (AMINO(L)HYDROXY(L)METHYL(L)ISOXAZOL?)
L54           6 S L51,L52
L55           2 S L54 AND L32
L56           2 S L31 AND L45,L48
L57           2 S L55,L56

     FILE 'REGISTRY' ENTERED AT 16:28:34 ON 30 APR 2001
L58           1 S 9042-64-2

     FILE 'HCAPLUS' ENTERED AT 16:28:40 ON 30 APR 2001
L59           1 S L32 AND L58
L60           1 S L32 AND ?DECARBOXYLASE?
L61           4 S L32,L57,L59,L60
L62          12 S L42 AND DYSKINES?
L63           3 S L42 AND TREMOR?
L64          49 S L42 AND ?PARKINSON?
L65           4 S L42 AND (CHOREA OR BALLISM OR DYSTON? OR ATHETO? OR MYOCLONUS
L66           6 S L42 AND MOTOR
L67           0 S L62-L66 AND L61
                E DYSKINES/CT
                E E5+ALL
L68          48 S  E1
L69         774 S E2
                E DYSKINES/CW
L70         136 S E4
L71           2 S L61 AND L68-L70
L72           4 S L61,L71
L73          14 S L64 AND L62,L63,L65,L66,L68-L70
L74       16997 S NMDA
L75        4925 S KAINIC ACID

     FILE 'REGISTRY' ENTERED AT 16:37:48 ON 30 APR 2001
L76           2 S 6384-92-5 OR 487-79-6
                E L-ASPARTIC ACID, N-METHYL-/CN
L77           1 S E3
                E DL-ASPARTIC ACID, N-METHYL-/CN
L78           1 S E3
                E 3-PYRROLIDINEACETIC ACID, 2-CARBOXY-4-(1-METHYLETHENYL)-/CN
L79           1 S E3
                E C10H15NO4/MF
L80          11 S E3 AND PYRROLIDINEACETIC AND CARBOXY AND METHYLETHENYL
L81          10 S L80 NOT T/ELS

     FILE 'HCAPLUS' ENTERED AT 16:40:21 ON 30 APR 2001
L82        8562 S L76-L79,L81
L83       11908 S  N()(METHYLASPARTIC OR METHYLASPARTATE OR METHYL(1W)(ASPARTIC
                E GLUTAMATE RECEPTOR/CT
                E E5+ALL
L84        7753 S E8+NT
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L85       25779 S L74,L75,L82-L84
L86         109 S SINEMET OR MADOPAR
L87         137 S L42,L86
L88           1 S L87 AND L85
L89           0 S L87 AND (L10 OR AMPA)

     FILE 'USPATFULL' ENTERED AT 16:44:15 ON 30 APR 2001
L90           1 S L25,L26

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FILE COVERS 1947 - 30 Apr 2001  VOL 134 ISS 19
FILE LAST UPDATED: 29 Apr 2001  (20010429/ED)

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 substance identification.

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information and abstracts were added for over 2.2 million references
published in CA from 1947 to 1966.


=> d all hitstr tot l72

L72  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2001 ACS
AN   1999:175749  HCAPLUS
DN   130:218317
TI   AMPA antagonists for the treatment of dyskinesias associated
     with dopamine agonist therapy
IN   Chenard, Bertrand Leo; Menniti, Frank Samuel;
     Welch, Willard McKowan, Jr.
PA   Pfizer Products Inc., USA
SO   Eur. Pat. Appl., 22 pp.
     CODEN: EPXXDW
DT   Patent
LA   English
IC   ICM  A61K031-505
ICI  A61K031-505, A61K031-195, A61K031-15
CC   1-11 (Pharmacology)
     Section cross-reference(s): 63
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
PI   EP 900568          A2   19990310       EP 1998-307181    19980904
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 11158072        A2   19990615       JP 1998-245269    19980831
     AU 9883120         A1   19990318       AU 1998-83120     19980904
     US 6136812         A    20001024       US 1998-148974    19980904
     CA 2246839         AA   19990305       CA 1998-2246839   19980908
PRAI US 1997-58098      P    19970905
```

OS MARPAT 130:218317

AB The invention relates to a method of treating dyskinesias assocd. with dopamine agonist therapy in a mammal which comprises administering to said mammal a compd., as defined herein, which is an antagonist of the **AMPA** receptor. Dopamine agonist therapy, as referred to in the present invention, is generally used in the treatment of a central nervous system disorder such as Parkinson's disease. One example compd. of the 212 claimed was (S)-3-(2-chlorophenyl)-2-[2-(5-diethylaminomethyl-2-fluorophenyl)vinyl]-6-fluoro-3H-quinazolin-4-one.

ST **AMPA** antagonist dyskinesia dopamine agonist

IT Drug delivery systems
Parkinson's disease
(**AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **AMPA** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **Dyskinesia (nervous system)**
(Parkinson's-assocd.; **AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 51-61-6, Dopamine, biological studies **59-92-7**, biological studies **322-35-0, Benserazide** 3257-47-4
28860-95-9, Carbidopa 199655-53-3 199655-54-4
199655-56-6 199655-57-7 199655-58-8 199655-59-9 199655-61-3
199655-62-4 199655-63-5 199655-64-6 199655-65-7 199655-66-8
199655-67-9 199655-68-0 199655-69-1 199655-70-4 199655-71-5
199655-72-6 199655-75-9 199655-76-0 199655-77-1 199655-78-2
199655-80-6 **199655-81-7** 199655-82-8 199655-84-0
199655-86-2 199655-87-3 199655-88-4 199655-89-5 199655-90-8
199655-91-9 199656-00-3 199656-44-5 212710-60-6 212710-61-7
212710-62-8 212710-64-0 212710-65-1 212710-66-2 212710-70-8
212765-03-2 212850-63-0 212850-64-1 212850-72-1 212850-74-3
212850-78-7 212850-79-8 212850-80-1 212850-81-2 212850-82-3
212916-59-1 212916-65-9 217821-32-4 217821-33-5 217821-34-6
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221177-89-5 221177-90-8 221177-91-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

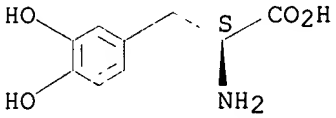
IT **77521-29-0, Ampa**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; **AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **9042-64-2, Dopa decarboxylase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; **AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

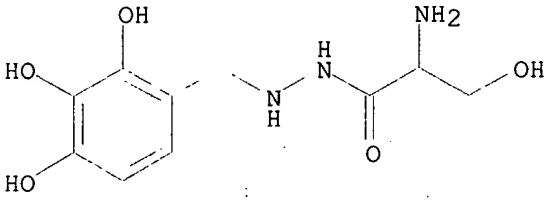
IT **59-92-7**, biological studies **322-35-0, Benserazide 28860-95-9, Carbidopa 199655-81-7**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (**AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

RN 59-92-7 HCAPLUS
CN L-Tyrosine, 3-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

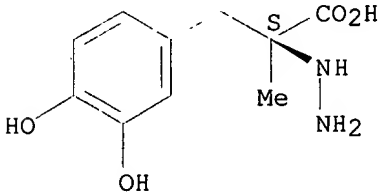


RN 322-35-0 HCAPLUS
CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)

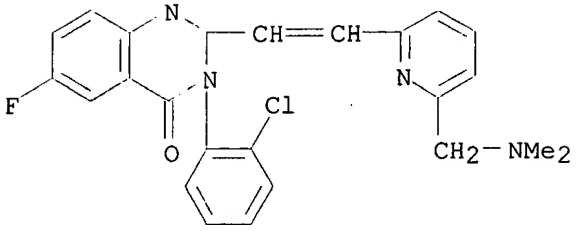


RN 28860-95-9 HCAPLUS
CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

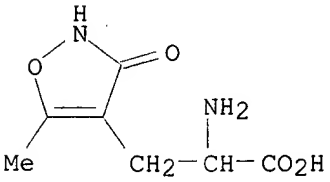
Absolute stereochemistry.



RN 199655-81-7 HCAPLUS
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



IT **77521-29-0, Ampa**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; **AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)
RN 77521-29-0 HCAPLUS
CN 4-Isoxazolepropanoic acid, .alpha.-amino-2,3-dihydro-5-methyl-3-oxo- (9CI) (CA INDEX NAME)



IT **9042-64-2, Dopa decarboxylase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)
RN 9042-64-2 HCAPLUS
CN Decarboxylase, aromatic amino acid (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L72 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:175748 HCAPLUS
DN 130:209717
TI Preparation of 3-(2-chlorophenyl)-2-[2-(6-diethylaminomethylpyridin-2-yl)vinyl]-6-fluoro-3H-quinazolin-4-one as an **AMPA** antagonist for the treatment of dyskinesias associated with dopamine agonist therapy.
IN **Chenard, Bertrand Leo; Greenamyre, John Timothy; Menniti, Frank Samuel; Welch, Willard McKowan, Jr.**
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K031-505
ICI A61K031-505, A61K031-195, A61K031-15
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 900567	A2	19990310	EP 1998-306661	19980820
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CA 2246560	AA	19990305	CA 1998-2246560	19980903
	JP 11139991	A2	19990525	JP 1998-249644	19980903
	AU 9883193	A1	19990318	AU 1998-83193	19980907
PRAI	US 1997-57965		19970905		

AB A method for the treatment of dyskinesias assocd. with dopamine agonist therapy comprising administration of an **AMPA** antagonist is

claimed (no data). Thus, 3-(2-chlorophenyl)-6-fluoro-2-methyl-4-(3H)-quinazolinone (prepn. given) was refluxed with 2,6-pyridinedicarboxaldehyde, ZnCl2, and Ac2O in dioxane to give 33% 6-[2-[3-(2-chlorophenyl)-6-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl]vinyl]pyridine-2-carboxaldehyde. This was stirred with Et2NH and NaBH(AcO)3 in CH2Cl2 to give 24% title compd. as the monomaleate salt.

ST chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone prepn **AMPA** antagonist; quinazolinone chlorophenyldiethylaminomethylpyrid inylvinyl prepn **AMPA** antagonist; dyskinesia treatment **AMPA** antagonist chlorophenyldiethylaminomethylpyridinylvinylfluoro quinazolinone

IT **AMPA** receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(antagonists; prepn. of chlorophenyldiethylaminomethylpyridinylvinylflu oroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **Dyskinesia (nervous system)**
(treatment; prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluor oquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **220931-86-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **199655-81-7**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **59-92-7**, L-**Dopa**, miscellaneous **322-35-0**, **Benserazide 28860-95-9**, **Carbidopa**
RL: MSC (Miscellaneous)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 95-51-2, 2-Chloroaniline 109-89-7, reactions 320-98-9 5431-44-7, 2,6-Pyridinedicarboxaldehyde
RL: RCT (Reactant)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 38520-78-4P 49579-12-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **220931-86-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

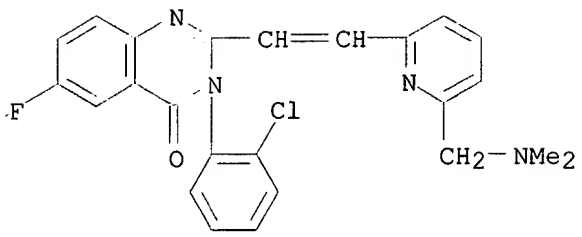
RN 220931-86-2 HCAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 199655-81-7

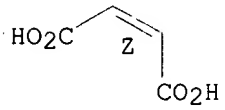
CMF C24 H20 Cl F N4 O



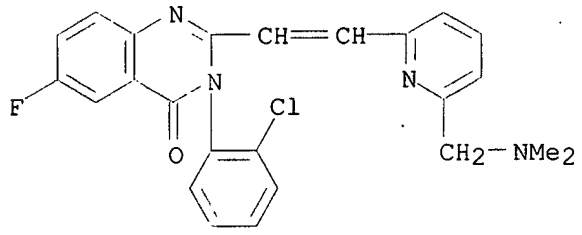
CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.

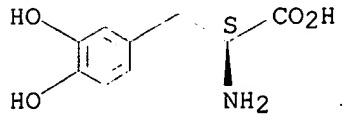


IT **199655-81-7**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
RN 199655-81-7 HCAPLUS
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)

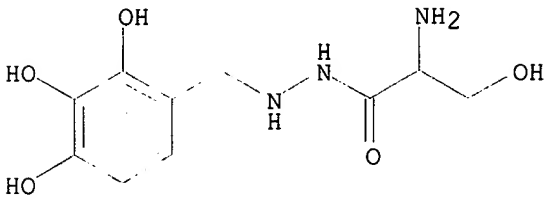


IT **59-92-7, L-Dopa**, miscellaneous **322-35-0, Benserazide 28860-95-9, Carbidopa**
RL: MSC (Miscellaneous)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
RN 59-92-7 HCAPLUS
CN L-Tyrosine, 3-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

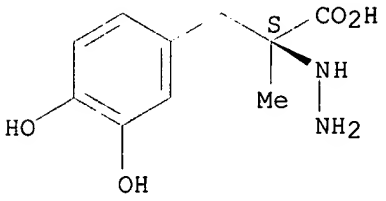


RN 322-35-0 HCAPLUS
CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)



RN 28860-95-9 HCAPLUS
CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

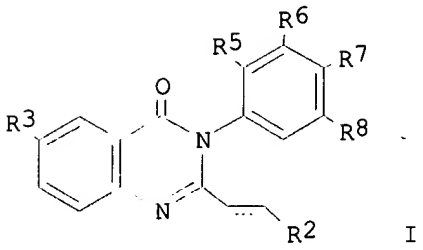
Absolute stereochemistry.



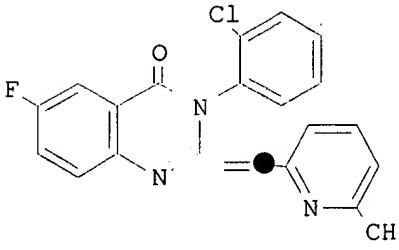
L72 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:608605 HCAPLUS
DN 129:230733
TI Preparation of atropisomers of 3-aryl-4(3H)-quinazolinones and their use as **AMPA**-receptor antagonists
IN **Welch, Willard McKowan, Jr.**; Devries, Keith M.
PA Pfizer Products Inc., USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D239-91
ICS C07D401-06; C07D417-06; C07D401-14; C07D405-06; C07D413-06; A61K031-505; C07M007-00
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9838173	A1	19980903	WO 1998-IB150	19980206
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9856768	A1	19980918	AU 1998-56768	19980206
	EP 968194	A1	20000105	EP 1998-900978	19980206
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	BR 9807872	A	20000321	BR 1998-7872	19980206
	JP 2000509731	T2	20000802	JP 1998-537448	19980206
	NO 9904177	A	19990827	NO 1999-4177	19990827
PRAI	US 1997-38905	P	19970228		
	WO 1998-IB150	W	19980206		

OS MARPAT 129:230733
GI



I



II

AB Title atropisomers [I; wherein R2 is an optionally substituted aryl or heteroaryl, R5 is alkyl, halo, CF3, alkoxy or alkylthio, R6, R7 and R8 are hydrogen or halo, and R3 is hydrogen, halo, CN, NO2, CF3, alkyl or alkoxy] are prepd. and are useful as **AMPA** receptor antagonists, particularly in the treatment of neurodegenerative and CNS-trauma related conditions (no data). The title (S)-atropisomer II was prepd. from 2-chloroaniline, 6-fluoro-2-methylquinoxalin-4-one which was prepd. from hydrogenation, acetylation, and cyclization of 2-nitro-5-fluorobenzoic acid, followed by reaction with 2,6-pyridinedicarboxaldehyde, and diethylamine, and was column sepd.

ST quinazolinone prepn; atropisomer quinazolinone sepn HPLC receptor antagonist

IT Separation
(HPLC column; prepn. and sepn. of atropisomers of arylquinazolinones as **AMPA**-receptor antagonists)

IT **AMPA** receptors
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antagonists; prepn. of atropisomers of arylquinazolinones as **AMPA**-receptor antagonists)

IT 212850-63-0P 212850-64-1P 212850-65-2P 212850-66-3P 212850-68-5P
212850-70-9P 212850-72-1P 212850-73-2P 212850-74-3P 212850-75-4P
212850-76-5P 212850-77-6P 212850-78-7P 212850-79-8P 212850-80-1P
212850-81-2P 212850-82-3P 212916-59-1P 212916-60-4P 212916-61-5P
212916-62-6P 212916-63-7P 212916-64-8P 212916-65-9P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of atropisomers of arylquinazolinones as **AMPA**-receptor antagonists)

IT 95-51-2, 2-Chloroaniline 109-89-7, Diethylamine, reactions 320-98-9
340-57-8 617-84-5, Diethylformamide 626-05-1, 2,6-Dibromopyridine
5431-44-7, 2,6-Pyridinedicarboxaldehyde 20949-84-2 27366-72-9
49579-01-3 49579-08-0 199656-43-4
RL: RCT (Reactant)

(prepn. of atropisomers of arylquinazolinones as **AMPA** -receptor antagonists)

IT 10200-43-8P 49579-12-6P 68683-04-5P 78441-69-7P 82586-66-1P
113732-84-6P 141567-53-5P 174608-36-7P 194473-04-6P 199599-68-3P
199655-35-1P 199655-36-2P 199655-54-4P 199655-55-5P 199655-57-7P
199655-61-3P 199655-62-4P 199655-63-5P 199655-65-7P 199655-66-8P
199655-67-9P 199655-68-0P 199655-69-1P 199655-70-4P 199655-71-5P
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199655-77-1P 199655-78-2P 199655-79-3P 199655-80-6P
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199655-86-2P 199655-87-3P 199655-88-4P 199655-89-5P 199655-90-8P
199655-91-9P 199655-92-0P 199655-93-1P 199655-96-4P 199655-97-5P
199655-98-6P 199655-99-7P 199656-02-5P 199656-03-6P 199656-04-7P
199656-05-8P 199656-06-9P 199656-28-5P 199656-29-6P 199656-30-9P
199656-31-0P 199656-32-1P 199656-33-2P 199656-34-3P 199656-35-4P
199656-40-1P 212764-92-6P 212764-93-7P 212764-94-8P 212764-95-9P
212764-96-0P 212764-97-1P 212764-99-3P 212765-00-9P 212765-01-0P
212765-02-1P 212765-03-2P 212765-05-4P 212765-06-5P 212765-07-6P
212765-08-7P 212765-09-8P 212765-10-1P 212765-11-2P 212765-12-3P
212765-13-4P 212765-15-6P 212765-16-7P 212765-19-0P 212765-20-3P
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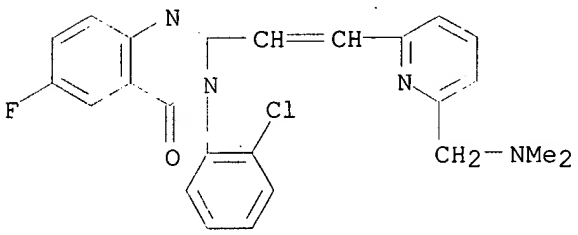
212765-26-9P 212765-27-0P 212765-28-1P 212772-14-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of atropisomers of arylquinazolinones as **AMPA** -receptor antagonists)

IT **199655-81-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of atropisomers of arylquinazolinones as **AMPA** -receptor antagonists)

RN 199655-81-7 HCAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



L72 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:752948 HCAPLUS

DN 128:34774

TI Preparation of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists.

IN Elliott, Mark Leonard; **Welch, Willard Mckowan Jr**

PA Pfizer Inc., USA; Elliott, Mark Leonard; Welch, Willard Mckowan Jr.

SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM C07D401-06
ICS C07D401-04; C07D401-14; C07D405-06; C07D403-06; C07D239-91; C07D417-14; C07D417-06; A61K031-505

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9743276	A1	19971120	WO 1997-IB134	19970217

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DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
MR, NE, SN, TD, TG

	CA 2252907	AA	19971120	CA 1997-2252907	19970217
	AU 9715549	A1	19971205	AU 1997-15549	19970217
	EP 901487	A1	19990317	EP 1997-901749	19970217
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	CN 1218464	A	19990602	CN 1997-194654	19970217
	BR 9709085	A	19990803	BR 1997-9085	19970217
	JP 11514663	T2	19991214	JP 1997-540682	19970217
	ZA 9704156	A	19981116	ZA 1997-4156	19970514
	NO 9805293	A	19990113	NO 1998-5293	19981113
PRAI	US 1996-17738		19960515		
	WO 1997-IB134		19970217		

OS MARPAT 128:34774
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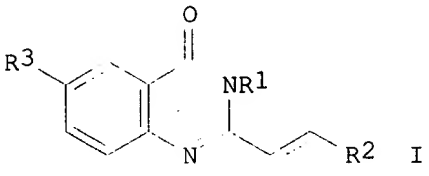

I

AB Title compds. [I; R1 = (substituted) Ph, pyridyl; R2 = (substituted) Ph, 5-6 membered heterocyclyl; R3 = H, halo, cyano, No2, CF3, alkyl, alkoxy], were prepd. Thus, 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylvinyl)-3H-quinazolin-4-one was hydrogenated in EtOAc over Pd/C to give 100% 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylethyl)-3H-quinazolin-4-one. Tested I inhibited **AMPA** receptor activation-induced 45Ca2+ uptake with IC50 <5 .mu.M.

ST quinazolinone prepn **AMPA** receptor antagonist; nervous system agents quinazolinone

IT Nervous system agents
Neurotransmitter antagonists
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

IT 3257-47-4P 199655-35-1P 199655-36-2P 199655-37-3P 199655-38-4P
199655-39-5P 199655-40-8P 199655-41-9P 199655-42-0P 199655-43-1P
199655-44-2P 199655-45-3P 199655-46-4P 199655-47-5P 199655-48-6P
199655-49-7P 199655-50-0P 199655-51-1P 199655-52-2P 199655-53-3P
199655-54-4P 199655-55-5P 199655-56-6P 199655-57-7P 199655-58-8P
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199655-64-6P 199655-65-7P 199655-66-8P 199655-67-9P 199655-68-0P
199655-69-1P 199655-70-4P 199655-71-5P 199655-72-6P 199655-73-7P
199655-74-8P 199655-75-9P 199655-76-0P 199655-77-1P 199655-78-2P
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199655-88-4P 199655-89-5P 199655-90-8P 199655-91-9P 199655-92-0P
199655-93-1P 199655-94-2P 199655-95-3P 199655-96-4P 199655-97-5P
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199656-23-0P 199656-24-1P 199656-25-2P 199656-26-3P 199656-27-4P

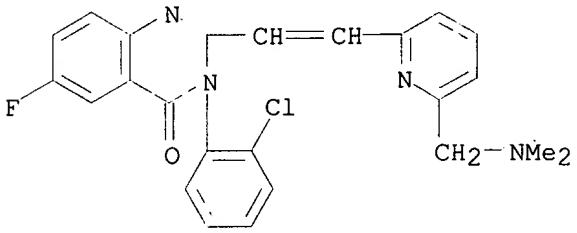
199656-28-5P 199656-29-6P 199656-30-9P 199656-31-0P 199656-32-1P
199656-33-2P 199656-34-3P 199656-35-4P 199656-36-5P 199656-37-6P
199656-38-7P 199656-39-8P 199656-40-1P 199656-41-2P 199656-44-5P
199656-45-6P 199656-46-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

IT 95-51-2, 2-Chloroaniline 320-98-9 340-57-8 5431-44-7, 2,6-Pyridinedicarboxaldehyde 20949-84-2, 2-Methylthiazole-4-carboxaldehyde 49579-01-3 49579-08-0 199599-68-3 199656-42-3 199656-43-4
RL: RCT (Reactant)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

IT 38520-78-4P 49579-12-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

IT **199655-81-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

RN 199655-81-7 HCAPLUS
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



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CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 24 Apr 2001 (20010424/PD)
FILE LAST UPDATED: 24 Apr 2001 (20010424/ED)
HIGHEST PATENT NUMBER: US6223348
CA INDEXING IS CURRENT THROUGH 24 Apr 2001 (20010424/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 24 Apr 2001 (20010424/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2000
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2000

>>> Page images are available for patents from 1/1/1997. Current <<<
>>> week patent text is typically loaded by Thursday morning and <<<
>>> page images are available for display by the end of the day. <<<
>>> Image data for the /FA field are available the following week. <<<

>>> Complete CA file indexing for chemical patents (or equivalents) <<<
>>> is included in file records. A thesaurus is available for the <<<
>>> USPTO Manual of Classifications in the /NCL, /INCL, and /RPCL <<<
>>> fields. This thesaurus includes catchword terms from the <<<
>>> USPTO/MOC subject headings and subheadings. Thesauri are also <<<
>>> available for the WIPO International Patent Classification <<<

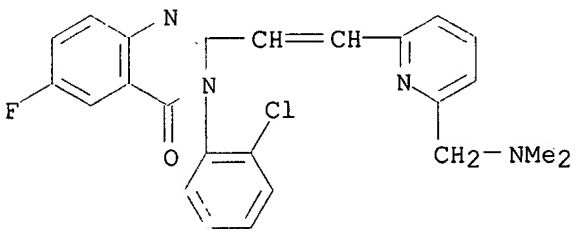
>>> (IPC) Manuals, editions 1-6, in the /IC1, /IC2, /IC3, /IC4, <<<
>>> /IC5, and /IC (/IC6) fields, respectively. The thesauri in <<<
>>> the /IC5 and /IC fields include the corresponding catchword <<<
>>> terms from the IPC subject headings and subheadings. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitstr l90

L90 ANSWER 1 OF 1 USPATFULL
AN 2000:142378 USPATFULL
TI Methods of administering AMPA receptor antagonists to treat dyskinesias associated with dopamine agonist therapy
IN Chenard, Bertrand L., Waterford, CT, United States
Welch, Willard M., Mystic, CT, United States
Menniti, Frank S., Mystic, CT, United States
PA Pfizer Inc, New York, NY, United States (U.S. corporation)
PI US 6136812 20001024
AI US 1998-148974 19980904 (9)
PRAI US 1997-58098 19970905 (60)
DT Utility
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Richardson, Peter C.; Ginsberg, Paul H.; Konstas, Kristina L.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2016
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a method of treating dyskinesias associated with dopamine agonist therapy in a mammal which comprises administering to said mammal a compound, as defined herein, which is an antagonist of the AMPA receptor. Dopamine agonist therapy, as referred to in the present invention, is generally used in the treatment of a central nervous system disorder such as Parkinson's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **199655-81-7**
(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)
RN 199655-81-7 USPATFULL
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



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DICTIONARY FILE UPDATES: 29 APR 2001 HIGHEST RN 333381-38-7

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

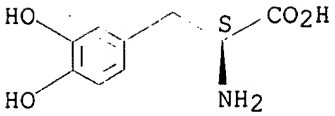
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> d ide can l14

L14 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN **59-92-7** REGISTRY
CN L-Tyrosine, 3-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Alanine, 3-(3,4-dihydroxyphenyl)-, L- (8CI)
OTHER NAMES:
CN (-)-3,4-Dihydroxyphenylalanine
CN (-)-Dopa
CN .beta.-(3,4-Dihydroxyphenyl)-.alpha.-L-alanine
CN .beta.-(3,4-Dihydroxyphenyl)-L-alanine
CN .beta.-(3,4-Dihydroxyphenyl)alanine
CN 3,4-Dihydroxy-L-phenylalanine
CN 3,4-Dihydroxyphenyl-L-alanine
CN 3,4-Dihydroxyphenylalanine
CN 3-(3,4-Dihydroxyphenyl)-L-alanine
CN 3-Hydroxy-L-tyrosine
CN DA
CN Dihydroxy-L-phenylalanine
CN DOPA
CN Dopaflex
CN Dopalina
CN Dopar
CN Dopaston
CN Dopaston SE
CN Eldopal
CN Helfo-dopa
CN Insulamina
CN L-(-)-Dopa
CN L-.beta.-(3,4-Dihydroxyphenyl)-.alpha.-alanine
CN L-3-(3,4-Dihydroxyphenyl)alanine
CN L-4,5-Dihydroxyphenylalanine
CN L-DOPA
CN Larodopa
CN Levodopa
CN Levopa
CN Pardopa
FS STEREOSEARCH
DR 25525-15-9, 23734-74-9, 72572-99-7, 72573-00-3, 90638-38-3, 88250-23-1, 34241-25-3
MF C9 H11 N O4
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



9109 REFERENCES IN FILE CA (1967 TO DATE)
260 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9123 REFERENCES IN FILE CAPLUS (1967 TO DATE)
17 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:265967

REFERENCE 2: 134:265203

REFERENCE 3: 134:262181

REFERENCE 4: 134:261267

REFERENCE 5: 134:261182

REFERENCE 6: 134:251260

REFERENCE 7: 134:249755

REFERENCE 8: 134:249215

REFERENCE 9: 134:247378

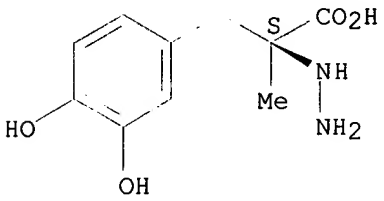
REFERENCE 10: 134:242762

=> d ide can l17

L17 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN **28860-95-9** REGISTRY
CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (S)-
CN Hydrocinnamic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, L- (8CI)
OTHER NAMES:
CN (-)-L-.alpha.-Hydrazino-3,4-dihydroxy-.alpha.-methylhydrocinamic acid
CN (-)-L-.alpha.-Hydrazino-3,4-dihydroxy-.alpha.-methylhydrocinnamic acid monohydrate
CN .alpha.-Hydrazino-.alpha.-methyl-.beta.-(3,4-dihydroxyphenyl)propionic acid
CN .alpha.-Methyldopahydrazine
CN 1-.alpha.-(3,4-Dihydroxybenzyl)-.alpha.-hydrazinopropionic acid
CN Carbidopa
CN Hydrazino-.alpha.-methyldopa
CN L-.alpha.-(3,4-Dihydroxybenzyl)-.alpha.-hydrazinopropionic acid
CN L-.alpha.-Hydrazino-.alpha.-methyl-.beta.-(3,4-dihydroxyphenyl)propionic acid
CN L-.alpha.-Hydrazino-.alpha.-methyl-3,4-dihydroxyphenylpropionic acid
CN L-.alpha.-Hydrazino-3,4-dihydroxy-.alpha.-methylbenzenepropanoic acid
CN L-.alpha.-Methyl-.alpha.-hydrazino-.beta.-(3,4-dihydroxyphenyl)propionic acid
CN L-.alpha.-Methyl-.alpha.-hydrazino-3,4-dihydroxyphenylpropionic acid
CN L-.alpha.-Methyl-.beta.-(3,4-dihydroxyphenyl)-.alpha.-hydrazinopropionic acid
CN L-.alpha.-Methyldopahydrazine
CN L-3-(3,4-Dihydroxyphenyl)-2-methyl-2-hydrazinopropionic acid

CN MK 486
CN N-Aminomethyldopa
FS STEREOSEARCH
DR 27925-91-3, 31823-41-3
MF C10 H14 N2 O4
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MRCK*, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



540 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
541 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:256873

REFERENCE 2: 134:242762

REFERENCE 3: 134:198100

REFERENCE 4: 134:188216

REFERENCE 5: 134:172697

REFERENCE 6: 134:168355

REFERENCE 7: 134:157584

REFERENCE 8: 134:157063

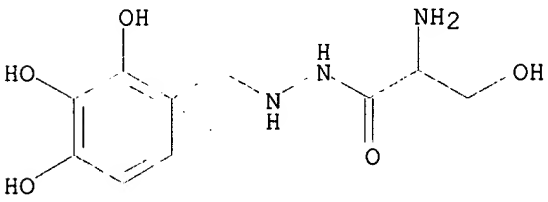
REFERENCE 9: 134:121022

REFERENCE 10: 134:120931

=> d ide can 120

L20 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN **322-35-0** REGISTRY
CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN DL-Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide
CN Serine, 2-(2,3,4-trihydroxybenzyl)hydrazide (7CI)
CN Serine, 2-(2,3,4-trihydroxybenzyl)hydrazide, DL- (8CI)
OTHER NAMES:
CN Benserazide
CN DL-Seryltrihydroxybenzylhydrazine
CN N-(DL-Seryl)-N'-(2,3,4-trihydroxybenzyl)hydrazine
CN N1-(DL-Seryl)-N2-(2,3,4-trihydroxybenzyl)hydrazine
CN N1-(DL-Seryl)-N2-(2,3,4-trihydroxybenzyl)hydrazine hydrochloride
CN Serazide

MF C10 H15 N3 O5
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



346 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
347 REFERENCES IN FILE CAPLUS (1967 TO DATE)
20 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:249866

REFERENCE 2: 134:188216

REFERENCE 3: 134:105933

REFERENCE 4: 134:95504

REFERENCE 5: 134:3509

REFERENCE 6: 133:325730

REFERENCE 7: 133:256811

REFERENCE 8: 133:227909

REFERENCE 9: 133:183136

REFERENCE 10: 133:182991

=> d ide can l40 tot

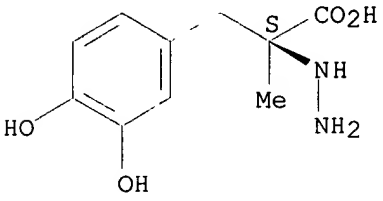
L40 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2001 ACS
RN 57308-51-7 REGISTRY
CN L-Tyrosine, 3-hydroxy-, mixt. with (.alpha.S)-.alpha.-hydrazino-3,4-dihydroxy-.alpha.-methylbenzenepropanoic acid (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (S)-, mixt. contg.
CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (.alpha.S)-, mixt. contg. (9CI)
CN L-Tyrosine, 3-hydroxy-, mixt. with (S)-.alpha.-hydrazino-3,4-dihydroxy-.alpha.-methylbenzenepropanoic acid
OTHER NAMES:
CN Carbidopa-L-dopa mixt.
CN Carbidopa-levodopa mixt.
CN Isicom
CN Nacom
CN Nakom
CN Sinemet
FS STEREOSEARCH

MF **C10 H14 N2 O4 . C9 H11 N O4**
CI MXS
LC STN Files: BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CIN, DIOGENES, EMBASE, IMSDIRECTORY, MEDLINE, MRCK*, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

CM 1

CRN 28860-95-9
CMF C10 H14 N2 O4

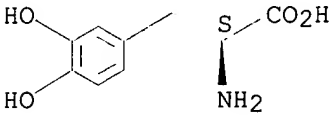
Absolute stereochemistry.



CM 2

CRN 59-92-7
CMF C9 H11 N O4

Absolute stereochemistry.



76 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
76 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:294727

REFERENCE 2: 133:204797

REFERENCE 3: 133:8986

REFERENCE 4: 131:165329

REFERENCE 5: 130:320759

REFERENCE 6: 130:261969

REFERENCE 7: 129:339741

REFERENCE 8: 129:301201

REFERENCE 9: 129:38404

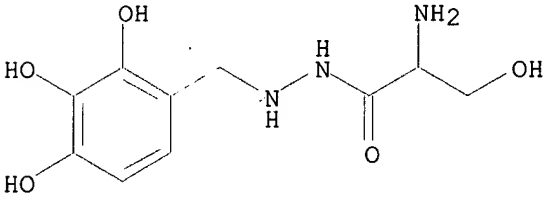
REFERENCE 10: 128:212698

L40 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2001 ACS
RN 37270-69-2 REGISTRY
CN L-Tyrosine, 3-hydroxy-, mixt. with serine 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN DL-Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide, mixt. contg.
CN L-Tyrosine, 3-hydroxy-, mixt. with DL-serine 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide
CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide, mixt. contg. (9CI)
OTHER NAMES:
CN Madopar
CN Ro 8-0576
FS STEREOSEARCH
DR 61949-25-5
MF **C10 H15 N3 O5 . C9 H11 N O4**
CI MXS
LC STN Files: BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CIN, EMBASE, IMSDIRECTORY, MEDLINE, MRCK*, PROMT, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

CM 1

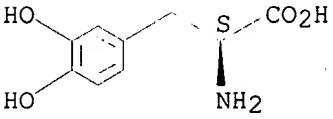
CRN 322-35-0
CMF C10 H15 N3 O5



CM 2

CRN 59-92-7
CMF C9 H11 N O4

Absolute stereochemistry.



33 REFERENCES IN FILE CA (1967 TO DATE)
33 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:294727

REFERENCE 2: 131:266533

REFERENCE 3: 130:7366

REFERENCE 4: 129:239731

REFERENCE 5: 127:272715

REFERENCE 6: 124:250675

REFERENCE 7: 123:275785

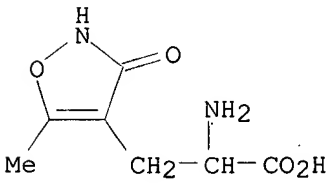
REFERENCE 8: 123:74239

REFERENCE 9: 123:782

REFERENCE 10: 122:96274

=> d ide can l9

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN **77521-29-0** REGISTRY
CN 4-Isoxazolepropanoic acid, .alpha.-amino-2,3-dihydro-5-methyl-3-oxo- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (.+-.)-.alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
CN (R,S)-.alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
CN (RS)-.alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
CN .alpha.-Amino-2,3-dihydro-5-methyl-3-oxoisoxazole-4-propionic acid
CN .alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionate
CN .alpha.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid
CN .gamma.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid
CN AMPA
CN AMPA (pharmaceutical)
CN D,L-.alpha.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid
CN dl-.alpha.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid
FS 3D CONCORD
DR 126632-03-9, 133481-32-0, 139261-99-7, 139559-02-7, 74341-63-2, 78729-80-3, 79697-77-1, 85506-19-0, 86495-63-8, 83354-19-2, 81323-87-7, 92614-50-1, 110592-37-5
MF C7 H10 N2 O4
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



982 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
982 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:264542

REFERENCE 2: 134:264541

REFERENCE 3: 134:202979

REFERENCE 4: 134:202883

REFERENCE 5: 134:190909

REFERENCE 6: 134:174165

REFERENCE 7: 134:173334

REFERENCE 8: 134:159650

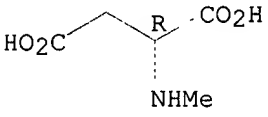
REFERENCE 9: 134:158014

REFERENCE 10: 134:158002

=> d ide can 176 tot

L76 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2001 ACS
RN **6384-92-5** REGISTRY
CN D-Aspartic acid, N-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Aspartic acid, N-methyl-, D- (8CI)
OTHER NAMES:
CN N-Methyl-D-aspartic acid
CN NMDA
FS STEREOSEARCH
MF C5 H9 N O4
CI COM
LC STN Files: AGRICOLA, AIDSLINE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, EMBASE, IFICDB, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



5598 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5603 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:264535

REFERENCE 2: 134:264523

REFERENCE 3: 134:264120

REFERENCE 4: 134:248974

REFERENCE 5: 134:247465

REFERENCE 6: 134:247458

REFERENCE 7: 134:232180

REFERENCE 8: 134:232146

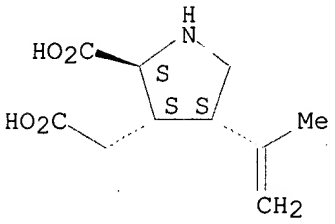
REFERENCE 9: 134:232134

REFERENCE 10: 134:232120

L76 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2001 ACS
RN **487-79-6** REGISTRY
CN 3-Pyrrolidineacetic acid, 2-carboxy-4-(1-methylethenyl)-, (2S,3S,4S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Pyrrolidineacetic acid, 2-carboxy-4-(1-methylethenyl)-, [2S-(2.alpha.,3.beta.,4.beta.)]-
CN 3-Pyrrolidineacetic acid, 2-carboxy-4-isopropenyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN (-)-.alpha.-Kainic acid
CN (-)-Kainic acid
CN (2S,3S,4S)-2-Carboxy-4-isopropenylpyrrolidine-3-acetic acid
CN .alpha.-Kainic acid

CN Digenic acid
CN Digenin
CN Helminal
CN Kainic acid
CN L-.alpha.-Kainic acid
FS STEREOSEARCH
DR 4071-38-9, 46398-96-3
MF C10 H15 N O4
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry. Rotation (-).



3858 REFERENCES IN FILE CA (1967 TO DATE)
41 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3863 REFERENCES IN FILE CAPLUS (1967 TO DATE)
26 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:264545

REFERENCE 2: 134:261996

REFERENCE 3: 134:235967

REFERENCE 4: 134:232143

REFERENCE 5: 134:232142

REFERENCE 6: 134:232141

REFERENCE 7: 134:232100

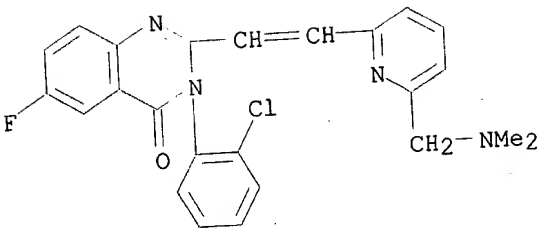
REFERENCE 8: 134:222008

REFERENCE 9: 134:220893

REFERENCE 10: 134:218095

=> d ide can l25

L25 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN **199655-81-7** REGISTRY
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H20 Cl F N4 O
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:218317

REFERENCE 2: 130:209717

REFERENCE 3: 129:230733

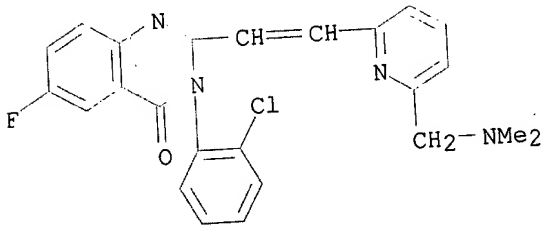
REFERENCE 4: 128:34774

=> d ide can 126

L26 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 220931-86-2 REGISTRY
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H20 Cl F N4 O . C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS

CM 1

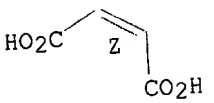
CRN 199655-81-7
CMF C24 H20 Cl F N4 O



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



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              1 REFERENCES IN FILE CA (1967 TO DATE)
              1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  130:209717


=> fil embase
FILE 'EMBASE' ENTERED AT 16:57:13 ON 30 APR 2001
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 FILE COVERS 1974 TO 19 Apr 2001 (20010419/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d his l91-

     (FILE 'HCAPLUS' ENTERED AT 16:44:40 ON 30 APR 2001)

     FILE 'USPATFULL' ENTERED AT 16:45:05 ON 30 APR 2001

     FILE 'REGISTRY' ENTERED AT 16:45:26 ON 30 APR 2001

     FILE 'EMBASE' ENTERED AT 16:48:07 ON 30 APR 2001
L91         2635 S L9
L92         2635 S ALPHA AMINO 3 HYDROXY 5 METHYL 4 ISOXAZOLEPROPIONIC ACID/CT
L93         5086 S L91,L92 OR AMPA
L94            0 S L25 OR L26
L95         2291 S L40
L96         1807 S CARBIDOPA PLUS LEVODOPA/CT
L97          928 S BENSERAZIDE PLUS LEVODOPA/CT
L98         1679 S SINEMET OR MADOPAR
L99            3 S L93 AND L95-L98
L100       19733 S L14-L16
L101        1913 S LEVODOPA(L)CB/CT
L102        3422 S L17-L19
L103         951 S CARBIDOPA(L)CB/CT
L104        2216 S L20,L24
L105         472 S BENSERAZIDE(L)CB/CT
L106        1178 S L101 AND L103,L105
L107           3 S L106 AND L93
L108           6 S (L100 OR LEVODOPA/CT) AND (L102 OR CARBIDOPA/CT OR L104 OR BE
L109           7 S L99,L107,L108
                 E AMPA RECEPTOR ANTAGONIST/CT
                 E E3+ALL
L110        5732 S E5+NT
L111          33 S (L100 OR LEVODOPA/CT) AND (L102 OR CARBIDOPA/CT OR L104 OR BE
L112           9 S (L100 OR LEVODOPA/CT) AND (L102 OR CARBIDOPA/CT OR L104 OR BE
L113          10 S L109,L112

     FILE 'EMBASE' ENTERED AT 16:57:13 ON 30 APR 2001

=> d all tot l113

L113 ANSWER 1 OF 10  EMBASE  COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN   2000150429  EMBASE
TI   AMPA receptor blockade improves levodopa-induced dyskinesia in
     MPTP monkeys.
AU   Konitsiotis S.; Blanchet P.J.; Verhagen L.; Lamers E.; Chase T.N.
CS   Dr. T.N. Chase, Experimental Therapeutics Branch, Building 10, Natl. Inst.
     Neurol. Disorders/Stroke, Bethesda, MD 20892-1406, United States.
     chase@helix.nih.gov
SO   Neurology, (2000) 54/8 (1589-1595).
     Refs: 49
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ISSN: 0028-3878 CODEN: NEURAI
CY United States
DT Journal; Article
FS 008 Neurology and Neurosurgery
037 Drug Literature Index
LA English
SL English
AB Objective: To evaluate the contribution of amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (**AMPA**) glutamate receptors to the pathogenesis of parkinsonian signs and levodopa-induced dyskinesias. Background: Motor fluctuations and dyskinesias reflect, in part, altered function of glutamate receptors of the NMDA subtype. The possible role of **AMPA** receptors, however, has not yet been examined. Methods: The authors compared the ability of an **AMPA** agonist (CX516) and a noncompetitive **AMPA** antagonist (LY300164) to alter parkinsonian symptoms and levodopa-induced dyskinesia in MPTP-lesioned monkeys. Eight levodopa-treated parkinsonian monkeys received rising doses of each drug, first in monotherapy and then in combination with low-, medium-, and high-dose levodopa. Results: CX516 alone, as well as when combined with low-dose levodopa, did not affect motor activity but induced dyskinesia. Moreover, following injection of the higher doses of levodopa, it increased levodopa-induced dyskinesia by up to 52% ($p < 0.05$). LY300164 potentiated the motor activating effects of low-dose levodopa, increasing motor activity by as much as 86% ($p < 0.05$), and that of medium-dose levodopa as much as 54% ($p < 0.05$). At the same time, LY300164 decreased levodopa-induced dyskinesia by up to 40% ($p < 0.05$). Conclusions: **AMPA** receptor upregulation may contribute to the expression of levodopa-induced dyskinesia. Conceivably, noncompetitive **AMPA** receptor antagonists could be useful, alone or in combination with NMDA antagonists, in the treatment of PD, by enhancing the antiparkinsonian effects of levodopa without increasing and possibly even decreasing levodopa- induced dyskinesia.
CT Medical Descriptors:
*dyskinesia: PC, prevention
*Parkinson disease: PC, prevention
pathogenesis
monkey
dose response
receptor upregulation
receptor blocking
combination chemotherapy
disease severity
nonhuman
male
female
animal model
controlled study
animal tissue
animal cell
article
priority journal
Drug Descriptors:
***AMPA receptor agonist: PD, pharmacology**
***AMPA receptor agonist: SC, subcutaneous drug administration**
***AMPA receptor antagonist: CB, drug combination**
***AMPA receptor antagonist: PD, pharmacology**
***AMPA receptor antagonist: SC, subcutaneous drug administration**
***levodopa: PD, pharmacology**
*n methyl dextro aspartic acid receptor blocking agent: CB, drug combination
*n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
6 quinoxalinecarboxylic acid piperidide: PD, pharmacology
talampanel: PD, pharmacology
benserazide: PD, pharmacology
RN (levodopa) **59-92-7**; (6 quinoxalinecarboxylic acid piperidide) 154235-83-3; (talampanel) 161832-65-1, 161832-67-3; (benserazide)

14919-77-8, **322-35-0**
CN (1) Cx 516; (2) Ly 300164
CO (1) Cortex (United States); (2) Lilly (United States); Research Biochemicals

L113 ANSWER 2 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 96027659 EMBASE
DN 1996027659
TI Some central effects of GYKI 52466, a non-competitive **AMPA** receptor antagonist.
AU Maj J.; Rogoz Z.; Skuza G.; Kolodziejczyk K.
CS Institute of Pharmacology, Polish Academy of Sciences, Smetna 12,31-343 Krakow, Poland
SO Polish Journal of Pharmacology, (1995) 47/6 (501-507).
ISSN: 1230-6002 CODEN: PJPAE3
CY Poland
DT Journal; Article
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB GYKI 52466 [1-(4-aminophenyl)-4-methyl-7,8-methylenedioxy-5H-2,3-benzodiazepine] has been described as a non-competitive **AMPA** (non-NMDA glutamate) receptor antagonist. In the present paper some behavioral effects of GYKI 52466 were studied in male Wistar rats and male Albino Swiss mice. GYKI 52466 reduced the locomotor activity in normal rats and mice, without evoking any symptoms of behavioral stimulation. The CGP 37849-induced hyperlocomotion was increased by GYKI 52466. The akinesia in monoamine-depleted rats was not affected by the drug studied. The antiakinetic effect of L-DOPA was not changed by GYKI 52466, whereas the antiakinetic effect of L-DOPA + CGP 37849 was decreased. GYKI 52466 increased the hyperlocomotion induced by apomorphine or cocaine. The drug did not change the catalepsy induced by haloperidol or fluphenazine, as well as the anticataleptic effect of CGP 37849. GYKI 52466 was inactive in the forced swimming test, but increased the antidepressant effect of CGP 37849. The flexor and extensor muscle tone of the rats hind limb was not modified by GYKI 52466. The results obtained indicate that GYKI 52466 shows a neuropharmacological profile similar but not identical with that of the quinoxalines (competitive **AMPA** receptor antagonists) studied previously.
CT Medical Descriptors:
*behavior
*central nervous system
akinesia
animal experiment
article
catalepsy
controlled study
drug antagonism
drug potentiation
extensor muscle
flexor muscle
forced swimming test
hyperactivity
intraperitoneal drug administration
locomotion
male
monoamine metabolism
mouse
muscle tone
nonhuman
rat
subcutaneous drug administration
Drug Descriptors:
***1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine:**

IT, drug interaction
***1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine: PD, pharmacology**
*quisqualic acid receptor: EC, endogenous compound
2 amino 4 methyl 5 phosphono 3 pentenoic acid: IT, drug interaction
2 amino 4 methyl 5 phosphono 3 pentenoic acid: CB, drug combination
2 amino 4 methyl 5 phosphono 3 pentenoic acid: PD, pharmacology
ampa receptor antagonist: PD, pharmacology
ampa receptor antagonist: IT, drug interaction
antidepressant agent: IT, drug interaction
antidepressant agent: PD, pharmacology
antidepressant agent: CB, drug combination
apomorphine: PD, pharmacology
apomorphine: IT, drug interaction
benserazide: PD, pharmacology
cocaine: IT, drug interaction
cocaine: PD, pharmacology
fluphenazine: PD, pharmacology
fluphenazine decanoate
glutamic acid antagonist: PD, pharmacology
glutamic acid antagonist: IT, drug interaction
haloperidol: PD, pharmacology
levodopa: IT, drug interaction
levodopa: PD, pharmacology
levodopa: CB, drug combination
metirosine: PD, pharmacology
quinoxaline derivative: PD, pharmacology
quinoxaline derivative: IT, drug interaction
reserpine: PD, pharmacology
RN (1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine) 102771-26-6; (2 amino 4 methyl 5 phosphono 3 pentenoic acid) 127910-31-0; (apomorphine) 314-19-2, 58-00-4; (benserazide) 14919-77-8, **322-35-0**; (cocaine) 50-36-2, 53-21-4, 5937-29-1; (fluphenazine) 146-56-5, 69-23-8; (fluphenazine decanoate) 5002-47-1; (haloperidol) 52-86-8; (levodopa) **59-92-7**; (metirosine) 672-87-7; (reserpine) 50-55-5, 8001-95-4
CN (1) Ro 4 4602; (2) Cgp 37849; (3) Lyogen; (4) Rausedyl
CO (1) Hoffmann la roche (Switzerland); (2) Ciba geigy (Switzerland); (3) Byk gulden (Germany); (4) Richter (Hungary); Sandoz (Switzerland); Merck (Germany); Reanal (Hungary); Institute for drug research (Hungary); Sigma (United States)

L113 ANSWER 3 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 95309948 EMBASE
DN 1995309948
TI Some behavioral effects of CNQX and NBQX, **AMPA** receptor antagonists.
AU Maj J.; Rogoz Z.; Skuza G.; Jaros T.
CS Institute of Pharmacology, Polish Academy of Sciences, Smetna 12,31-343 Krakow, Poland
SO Polish Journal of Pharmacology, (1995) 47/4 (269-277).
ISSN: 1230-6002 CODEN: PJPAE3
CY Poland
DT Journal; Article
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB CNQX (6-cyano-7-nitroquinoxaline-2,3-dione) and NBQX (2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo[f]quinoxaline), two competitive **AMPA** (non-NMDA glutamate) receptor antagonists, as well as their interaction with CGP 37849, a competitive NMDA receptor antagonist, were studied in rats and mice. CNQX and NBQX inhibited the locomotor activity of naive rats. No symptoms of behavioral excitation were observed. CGP 37849 induced locomotor hyperactivity which was reduced by CNQX and NBQX. In

monoamine-depleted rats (pretreated with reserpine + .alpha.-methyl-p-tyrosine), none of the two quinoxalines nor CGP 37849 antagonized akinesia. The antiakinetic effect of L-DOPA was increased by CGP 37849, but not by CNQX or NBQX. The latter action of CGP 37849 was decreased by CNQX and NBQX. The antiakinetic effect of clonidine was not changed by CNQX. The locomotor hyperactivity induced by apomorphine or cocaine was not modified by CNQX. Neither of the quinoxalines changed the catalepsy induced by haloperidol or spiperone. The fluphenazine catalepsy was slightly decreased by CNQX and increased by NBQX. CNQX and NBQX were inactive in the forced swimming test; CNQX (but not NBQX) increased the CGP 37849-induced reduction of the immobility time. CNQX decreased the muscle tone of hind limbs in naive and monoamine-depleted rats. The obtained results indicate that the **AMPA** receptor antagonists differ in their neuropharmacological profile from CGP 37849, an NMDA receptor antagonist. There is no positive cooperation (except for the forced swimming test) between NMDA and **AMPA** receptor antagonists; on the contrary, an antagonistic interaction between them has been observed.

CT Medical Descriptors:
*behavior
akinesia
animal experiment
animal model
article
controlled study
drug antagonism
drug potentiation
forced swimming test
hyperactivity
intraperitoneal drug administration
locomotion
male
monoamine metabolism
mouse
muscle tone
nonhuman
rat
subcutaneous drug administration
Drug Descriptors:
*quisqualic acid receptor
*2 amino 4 methyl 5 phosphono 3 pentenoic acid: IT, drug interaction
*2 amino 4 methyl 5 phosphono 3 pentenoic acid: PD, pharmacology
***6 cyano 7 nitro 2,3 quinoxalinedione: IT, drug interaction**
***6 cyano 7 nitro 2,3 quinoxalinedione: PD, pharmacology**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: IT, drug interaction**
*glutamic acid antagonist: PD, pharmacology
*glutamic acid antagonist: IT, drug interaction
*n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
*n methyl dextro aspartic acid receptor blocking agent: IT, drug interaction
ampa receptor antagonist: PD, pharmacology
ampa receptor antagonist: IT, drug interaction
apomorphine: PD, pharmacology
benserazide: CB, drug combination
benserazide: PD, pharmacology
clonidine: PD, pharmacology
cocaine: PD, pharmacology
fluphenazine: PD, pharmacology
fluphenazine: IT, drug interaction
fluphenazine decanoate
haloperidol: PD, pharmacology
levodopa: CB, drug combination
levodopa: IT, drug interaction

levodopa: PD, pharmacology
metirosine: PD, pharmacology
quinoxaline derivative: PD, pharmacology
quinoxaline derivative: IT, drug interaction
reserpine: PD, pharmacology
spiperone: PD, pharmacology
RN (2 amino 4 methyl 5 phosphono 3 pentenoic acid) 127910-31-0; (6 cyano 7 nitro 2,3 quinoxalinedione) 115066-14-3; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (apomorphine) 314-19-2, 58-00-4; (benserazide) 14919-77-8, **322-35-0**; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (cocaine) 50-36-2, 53-21-4, 5937-29-1; (fluphenazine) 146-56-5, 69-23-8; (fluphenazine decanoate) 5002-47-1; (haloperidol) 52-86-8; (levodopa) **59-92-7**; (metirosine) 672-87-7; (reserpine) 50-55-5, 8001-95-4; (spiperone) 749-02-0
CN (1) Cgp 37849; (2) Lyogen; (3) Rausedyl; (4) Ro 4 4602
CO (1) Ciba geigy (Switzerland); (2) Byk gulden (Germany); (3) Richter (Hungary); (4) Hoffmann la roche (Switzerland); Sandoz (Switzerland); Rbi (United States); Reanal (Hungary); Sigma (United States); Novo nordisk (Denmark)

L113 ANSWER 4 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 95119361 EMBASE
DN 1995119361
TI Modulation of dopamine D1-mediated tuning behavior and striatal c-fos expression by the substantia nigra.
AU Fenu S.; Carta A.; Morelli M.
CS Department of Toxicology, Viale A. Diaz 182,09100 Cagliari, Italy
SO Synapse, (1995) 19/4 (233-240).
ISSN: 0887-4476 CODEN: SYNAET
CY United States
DT Journal; Article
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
052 Toxicology
LA English
SL English
AB In order to study the possible contribution of the substantia nigra (SN) in the positive interaction between dopamine D1 receptor agonists and glutamate antagonists in unilaterally 6-hydroxydopamine (6-OHDA) lesioned rats, the effect of the D1 agonist, SKF 38393, was studied in combination with intranigral infusions of glutamate antagonists of the NMDA (MK 801, CPP) or **AMPA** (NBQX) type of receptor. Local infusion into the SN of the 6-OHDA lesioned side of MK 801, CPP or NBQX at doses inducing no or minimal behavioral effects significantly increased the turning behavior and the expression of c-fos induced, in the lesioned caudate-putamen (CPu), by a parenteral administration of SKF 38393. The same result was obtained after intra-SN infusion of the GABA agonist, muscimol. High doses of MK 801, CPP or muscimol infused into the SN produced intense contralateral turning per se and induced a sparse c-fos expression in the lesioned CPu which was antagonized by parenteral administration of MK 801. The results indicate that a depression of SN pars reticulata efferent neurons potentiates D1-mediated responses and suggest that this area may play a role in the positive interaction between glutamate antagonists and D1 receptor agonists.
CT Medical Descriptors:
*substantia nigra
animal behavior
animal experiment
animal tissue
article
caudate nucleus
controlled study
drug infusion
gene expression

immunohistochemistry
intracerebral drug administration
intravenous drug administration
male
neuropharmacology
nonhuman
oncogene c fos
priority journal
putamen
rat
Drug Descriptors:
*dopamine 1 receptor
n methyl dextro aspartic acid receptor
quisqualic acid receptor
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: CB, drug combination
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: PD, pharmacology
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: IT, drug interaction
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: DO, drug dose
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: CM, drug comparison
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CM, drug comparison**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: IT, drug interaction**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DO, drug dose**
*dizocilpine: DO, drug dose
*dizocilpine: IT, drug interaction
*dizocilpine: PD, pharmacology
*dizocilpine: CM, drug comparison
*dizocilpine: CB, drug combination
*dopamine 1 receptor blocking agent: DO, drug dose
*dopamine 1 receptor blocking agent: IT, drug interaction
*dopamine 1 receptor blocking agent: PD, pharmacology
*dopamine 1 receptor blocking agent: CM, drug comparison
*dopamine 1 receptor blocking agent: CB, drug combination
*glutamic acid antagonist: IT, drug interaction
*glutamic acid antagonist: DO, drug dose
*glutamic acid antagonist: CM, drug comparison
*glutamic acid antagonist: CB, drug combination
*glutamic acid antagonist: PD, pharmacology
4 aminobutyric acid receptor stimulating agent: CB, drug combination
4 aminobutyric acid receptor stimulating agent: PD, pharmacology
4 aminobutyric acid receptor stimulating agent: IT, drug interaction
4 aminobutyric acid receptor stimulating agent: DO, drug dose
4 aminobutyric acid receptor stimulating agent: CM, drug comparison
benserazide
desipramine
levodopa
muscimol: DO, drug dose
muscimol: PD, pharmacology
muscimol: IT, drug interaction
muscimol: CB, drug combination
muscimol: CM, drug comparison
n methyl dextro aspartic acid receptor blocking agent: CM, drug comparison
n methyl dextro aspartic acid receptor blocking agent: CB, drug combination
n methyl dextro aspartic acid receptor blocking agent: IT, drug interaction
n methyl dextro aspartic acid receptor blocking agent: DO, drug dose

n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
oxidopamine: TO, drug toxicity
RN (2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine) 67287-49-4; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (dizocilpine) 77086-21-6; (benserazide) 14919-77-8, **322-35-0**; (desipramine) 50-47-5, 58-28-6; (levodopa) **59-92-7**; (muscimol) 2763-96-4; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0
CN (1) Skf 38393; (2) Mk 801
CO (2) Rbi (United States); Hoffmann la roche (Switzerland); Ciba geigy (Switzerland); Sigma (Italy); Novo nordisk (Denmark)

L113 ANSWER 5 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 94097346 EMBASE
DN 1994097346
TI Excitatory amino acid receptor antagonists modify regional cerebral metabolic responses to levodopa in 6-hydroxydopamine-lesioned rats.
AU Engber T.M.; Anderson J.J.; Boldry R.C.; Papa S.M.; Kuo S.; Chase T.N.
CS Experimental Therapeutics Branch, NINDS,Bethesda, MD 20892, United States
SO Neuroscience, (1994) 59/2 (389-399).
ISSN: 0306-4522 CODEN: NRSCDN
CY United Kingdom
DT Journal; Article
FS 002 Physiology
008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Excitatory amino acid receptor antagonists have been proposed as novel therapeutic agents to be used with levodopa in the treatment of Parkinson's disease. We examined the neural substrates for the interaction between levodopa and antagonists of either the .alpha.-amino-3-hydroxy-5-methylisoxazole- 4-propionic acid or N-methyl-D-aspartate type of excitatory amino acid receptor using 2-deoxyglucose autoradiography. Thus, we compared the effects of the .alpha.-amino-3-hydroxy-5-methylisoxazole-4-propionic acid receptor antagonist 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F)quinoxaline (10 mg/kg, i.v.) and the N-methyl-D-aspartate antagonist MK-801 (0.1 mg/kg, i.v.) on cerebral metabolic responses to levodopa (25 mg/kg, i.v. with 12.5 mg/kg benserazide) in rats with a unilateral nigrostriatal pathway lesion. Levodopa increased glucose utilization ipsilateral to the lesion in substantia nigra pars reticula (up to 104%), entopeduncular nucleus (up 90%) and subthalamic nucleus (up 30%), indicating that levodopa alters striatal output through the striatonigral, striatoentopeduncular and striatopallidal pathways. Levodopa also decreased metabolic rate in lateral habenula (down 39%), a target of projections from entopeduncular nucleus, implying a reduction in basal ganglia output. 2,3-Dihydroxy-6-nitro-7-sulfamoyl-benzo(F)quinoxaline and MK- 801 by themselves did not affect glucose utilization in any of these regions. Pretreatment with 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F)quinoxaline reduced the effect of levodopa in substantia nigra pars reticulata but not in entopeduncular nucleus or subthalamic nucleus, while MK-801 attenuated the effect of levodopa in all three of these structures; neither 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F)quinoxaline nor MK-801 altered the effect of levodopa in lateral habenula. When given at the same doses to a separate group of lesioned animals, neither 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F)quinoxaline nor MK-801 affected rotational behavior elicited by levodopa. These findings indicate that .alpha.-amino-3-hydroxy-5-methylisoxazole- 4-propionic acid and N-methyl-D-aspartate receptor antagonists differentially modify dopamine receptor-mediated striatal output. .alpha.-Amino-3-hydroxy-5- methylisoxazole-4-propionic acid receptor blockade may preferentially attenuate the effect of dopamine receptor activation on the striatonigral pathway, while N-methyl-D-aspartate blockade appears to reduce the actions of dopamine on the striatonigral, striatoentopeduncular and striatopallidal pathways. However, the lack of effect of both 2,3-dihydroxy-6-nitro-7-

sulfamoyl-benzo(F)quinoxaline and MK-801 on levodopa-induced rotational behavior and reduced metabolic rate in the lateral habenula suggests that neither .alpha.-amino-3-hydroxy-5-methylisoxazole-4-propionic acid nor N-methyl- D-aspartate receptor blockade diminishes the net effect of levodopa on basal ganglia output.

CT Medical Descriptors:
*nigroneostriatal system
animal experiment
animal model
animal tissue
article
autoradiography
brain region
circling behavior
controlled study
intravenous drug administration
male
nonhuman
parkinson disease: DT, drug therapy
priority journal
rat
Drug Descriptors:
*dopamine receptor
*glutamate receptor
*n methyl dextro aspartic acid receptor
quisqualic acid receptor
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CM, drug comparison**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: IT, drug interaction**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology**
*deoxyglucose
*dizocilpine: CB, drug combination
*dizocilpine: CM, drug comparison
*dizocilpine: IT, drug interaction
*dizocilpine: PD, pharmacology
*glutamic acid antagonist: PD, pharmacology
*glutamic acid antagonist: CB, drug combination
*glutamic acid antagonist: CM, drug comparison
*glutamic acid antagonist: IT, drug interaction
***levodopa: IT, drug interaction**
***levodopa: PD, pharmacology**
*oxidopamine: TO, drug toxicity
benserazide: CB, drug combination

RN (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (deoxyglucose) 154-17-6; (dizocilpine) 77086-21-6; (levodopa) **59-92-7**; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0; (benserazide) 14919-77-8, **322-35-0**

CN (1) Mk 801

CO (1) Rbi (United States); Sigma (United States); Novo nordisk (Denmark); Hoffmann la roche (United States)

L113 ANSWER 6 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 94039675 EMBASE

DN 1994039675

TI The **AMPA** antagonists NBQX and GYKI 52466 do not counteract neuroleptic- induced catalepsy.

AU Zadow B.; Schmidt W.J.

CS Neuropharmacology Division, Zoological Institute, University of Tubingen, Mohlstrasse 54/1,D-72074 Tubingen, Germany

SO Naunyn-Schmiedeberg's Archives of Pharmacology, (1994) 349/1 (61-65). ISSN: 0028-1298 CODEN: NSAPCC

CY Germany

DT Journal; Article
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The **AMPA** antagonists NBQX (2.5, 5, 10 mg/kg) and GYKI 52466 (4.8, 8 mg/kg) were investigated in haloperidol (0.5 mg/kg)-induced catalepsy in the rat. The effects of **AMPA** antagonists administered either alone or in combination with the noncompetitive NMDA antagonist dizocilpine (0.02 mg/kg), with the dopamine D-2 agonist quinpirole (1 mg/kg) or with L-DOPA (50, 100 mg/kg plus benserazide) were tested. NBQX or GYKI 52466 did not exert anticataleptic effects, neither alone nor in combination with dizocilpine, quinpirole or L- DOPA. Thus, in the rat inhibition of **AMPA** receptors with NBQX or GYKI 52466 does not have effects predictive for an antiparkinsonian potential.
CT Medical Descriptors:
*catalepsy
animal experiment
article
controlled study
intraperitoneal drug administration
male
nonhuman
oral drug administration
rat
Drug Descriptors:
*excitatory amino acid receptor
quisqualic acid receptor
***1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine: PD, pharmacology**
***1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine: DO, drug dose**
***1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine: CB, drug combination**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DO, drug dose**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology**
*amino acid receptor blocking agent: CB, drug combination
*amino acid receptor blocking agent: DO, drug dose
*amino acid receptor blocking agent: PD, pharmacology
***benserazide: CB, drug combination**
*neuroleptic agent: PD, pharmacology
ampa receptor antagonist: CB, drug combination
ampa receptor antagonist: DO, drug dose
ampa receptor antagonist: PD, pharmacology
benserazide plus levodopa: PD, pharmacology
benserazide plus levodopa: CB, drug combination
dizocilpine: PD, pharmacology
dizocilpine: CB, drug combination
dopamine 2 receptor stimulating agent: CB, drug combination
dopamine 2 receptor stimulating agent: PD, pharmacology
levodopa: CB, drug combination
quinpirole: CB, drug combination
quinpirole: PD, pharmacology
RN (1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine) 102771-26-6; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (benserazide) 14919-77-8, **322-35-0**; (benserazide plus levodopa) **37270-69-2**; (dizocilpine) 77086-21-6; (levodopa) **59-92-7**; (quinpirole) 73625-62-4, 80373-22-4, 85760-75-4, 85798-08-9
CN (1) Mk 801; **(2) Madopar**; (3) Gyki 52466
CO (1) Merck sharp and dohme (Germany); (2) Hoffmann la roche (Germany); (3) Institute for drug research (Hungary); Novo nordisk (Denmark); Janssen

(Germany); Biotrend (Germany)

L113 ANSWER 7 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 93131307 EMBASE
DN 1993131307
TI Glutamate-dopamine interactions in the basal ganglia: Relationship to Parkinson's disease.
AU Greenamyre J.T.
CS Department of Neurology, University of Rochester, 601 Elmwood Ave,Rochester, NY 14642, United States
SO Journal of Neural Transmission - General Section, (1993) 91/2-3 (255-269). ISSN: 0300-9564 CODEN: JNTMAH
CY Austria
DT Journal; General Review
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Current antiparkinsonian therapies focus on either replacing dopamine via precursor (L-DOPA) administration, or directly stimulating postsynaptic dopamine receptors with dopamine agonists. Unfortunately, this approach is associated with numerous side effects and these drugs lose efficacy with disease progression. This article reviews recent evidence which suggests that negative modulation of glutamatergic neurotransmission has antiparkinsonian effects in a variety of rodent and primate models of parkinsonism. The pronounced synergism between dopaminergic agents and glutamate receptor antagonists may provide a means of using very low doses of the two drug classes in concert to treat Parkinson's disease effectively and minimize dose-related drug side effects.
CT Medical Descriptors:
*basal ganglion
*parkinson disease: ET, etiology
*parkinson disease: DT, drug therapy
animal model
disease course
drug effect
drug efficacy
drug potentiation
functional anatomy
modulation
neuroanatomy
neurotransmission
nonhuman
primate
priority journal
review
rodent
side effect
subthalamic nucleus
Drug Descriptors:
dopamine receptor
n methyl dextro aspartic acid receptor
*dopamine: EC, endogenous compound
*glutamic acid: EC, endogenous compound
1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: PD, pharmacology
1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: DT, drug therapy
6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology
6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DT, drug therapy
6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination
carbidopa: PD, pharmacology
carbidopa: CB, drug combination
dopamine receptor stimulating agent: DT, drug therapy
dopamine receptor stimulating agent: IT, drug interaction

dopamine receptor stimulating agent: DO, drug dose
dopamine receptor stimulating agent: CB, drug combination
dopamine receptor stimulating agent: AE, adverse drug reaction
glutamic acid antagonist: CB, drug combination
glutamic acid antagonist: DO, drug dose
glutamic acid antagonist: IT, drug interaction
glutamic acid antagonist: DT, drug therapy
levodopa: PD, pharmacology
levodopa: DT, drug therapy
levodopa: CB, drug combination
levodopa: AE, adverse drug reaction

RN (dopamine) 51-61-6, 62-31-7; (glutamic acid) 11070-68-1, 138-15-8, 56-86-0, 6899-05-4; (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine) 28289-54-5; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (carbidopa) **28860-95-9**; (levodopa) **59-92-7**

L113 ANSWER 8 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 93058820 EMBASE
DN 1993058820
TI Excitatory amino acid antagonists and Parkinson's disease.
AU Rosario Luquin M.; Martinez-Lage J.M.
CS Department Neurology/Neurosurgery, Clinica Universitaria, Medical School,Pamplona, Spain
SO New Trends in Clinical Neuropharmacology, (1992) 6/1-4 (43-47). ISSN: 0393-5345 CODEN: NTCNEP
CY Italy
DT Journal; Article
FS 008 Neurology and Neurosurgery
052 Toxicology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB We have studied the motor response induced by the administration of the **AMPA**-antagonist NBQX given alone or simultaneously with l-dopa to 2 parkinsonian monkeys. NBQX (1, 2 and 4 mg/kg im) failed to reverse parkinsonism. Similarly, co-administration of NBQX (1 mg/kg) plus l-dopa (12.5, 25 and 50 mg orally) did not modify the motor improvement and dyskinesia induced by l-dopa. These results suggest that NBQX can not be considered as a useful treatment for Parkinson's disease.
CT Medical Descriptors:
*motor dysfunction
*parkinson disease: DT, drug therapy
animal experiment
animal model
article
controlled study
dyskinesia
intramuscular drug administration
monkey
nonhuman
oral drug administration
Drug Descriptors:
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DO, drug dose**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DT, drug therapy**
***6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology**
*amino acid receptor blocking agent: PD, pharmacology
*amino acid receptor blocking agent: DT, drug therapy
*amino acid receptor blocking agent: DO, drug dose
*amino acid receptor blocking agent: CB, drug combination
***levodopa: CB, drug combination**
***levodopa: DT, drug therapy**

***levodopa: PD, pharmacology**
***levodopa: TO, drug toxicity**
***levodopa: DO, drug dose**
1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: TO, drug toxicity
benserazide: DT, drug therapy
benserazide: CB, drug combination
benserazide plus levodopa
naxagolide: DT, drug therapy
RN (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (levodopa) **59-92-7**; (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine) 28289-54-5; (benserazide) 14919-77-8, **322-35-0**; (benserazide plus levodopa) **37270-69-2**; (naxagolide) 88058-88-2
CN **(1) Madopar**
CO (1) Hoffmann la roche; Novo nordisk

L113 ANSWER 9 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 91340439 EMBASE
DN 1991340439
TI The **AMPA** receptor antagonist NBQX has antiparkinsonian effects in monoamine-depleted rats and MPTP-treated monkeys.
AU Klockgether T.; Turski L.; Honore T.; Zhang Z.; Gash D.M.; Kurlan R.; Greenamyre J.T.
CS Department of Neurology, Rochester Univ. Medical Center, Box 673, 601 Elmwood Ave,Rochester, NY 14642, United States
SO Annals of Neurology, (1991) 30/5 (717-723).
ISSN: 0364-5134 CODEN: ANNED3
CY United States
DT Journal; Article
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Abnormally increased subthalamic nucleus output to the internal pallidal segment and the reticular part of the substantia nigra plays a critical pathophysiological role in the development of parkinsonism. Because synaptic transmission of subthalamic output is glutamatergic and mediated, in part, by the .alpha.-amino-3-hydroxy-5-methyl-4-isoxazole propionate (**AMPA**) subtype of glutamate receptor, **AMPA** receptor antagonists may possess antiparkinsonian properties. We report that in monoamine-depleted rats, 2,3-dihydroxy-6-nitro-7-sulfamoyl-bonzo(f)quinoxaline (NBQX) (Novo-Nordisk, Copenhagen, Denmark)-a selective antagonist of the **AMPA** subtype of glutamate receptor-suppressed muscular rigidity but had no effect on akinesia. NBQX microinjected into the subthalamic nucleus, internal pallidal segment, and reticular part of the substantia nigra, but not into the laterodorsal neostriatum of the rats, stimulated locomotor activity and reduced muscular rigidity. In aged Rhesus monkeys with bilateral 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced parkinsonism, intramuscular NBQX produced clinically apparent improvement in akinesia, tremor, posture, and gross motor skills. NBQX also potentiated the antiparkinsonian effects of L-3,4-dihydroxyphenylalanine in both rats and monkeys. Blockade of excitatory synaptic transmission by **AMPA** receptor antagonists may provide a new therapeutic strategy for Parkinson's disease (PD).
CT Medical Descriptors:
*parkinsonism
*rigidity
animal model
article
female
intramuscular drug administration
male
monkey
nonhuman
priority journal
Drug Descriptors:

*1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine
*reserpine
6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione
carbidopa plus levodopa
RN (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine) 28289-54-5; (reserpine) 50-55-5, 8001-95-4; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (carbidopa plus levodopa) **57308-51-7**
CN **(1) Sinemet**
CO (1) Merck sharp and dohme; Novo nordisk (Denmark)

L113 ANSWER 10 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 80251895 EMBASE
DN 1980251895
TI Kainic acid-induced wet dog shakes in rats. The relation to central neurotransmitters.
AU Kleinrok Z.; Turski L.
CS Dept. Pharmacol., Inst. Clin. Pathol., Med. Sch., PL-20-090 Lublin, Poland
SO Naunyn-Schmiedeberg's Archives of Pharmacology, (1980) 314/1 (37-46). CODEN: NSAPCC
CY Germany
DT Journal
FS 030 Pharmacology
050 Epilepsy
037 Drug Literature Index
008 Neurology and Neurosurgery
LA English
AB Following the intracerebroventricular administration of kainic acid (KA), rats showed wet dog shakes (WDS) in a dose-dependent manner. DL-.alpha.-aminoadipic acid and L-glutamic acid diethylester blocked WDS behavior induced by 0.05 .mu.g of KA. Noradrenaline, clonidine, yohimbine and apomorphine also significantly blocked KA-induced WDS. Phentolamine and propranolol did not affect WDS. FLA 63, 6-OHDA lesion and bilateralis electrolytic lesion to locus coeruleus markedly enhanced, but L-Dopa blocked WDS behavior. Moreover, the KA-induced shaking behavior was blocked by .alpha.-methyl-p-tyrosine and haloperidol. Cyproheptadine and methergoline also blocked WDS. p-Chlorophenylalanine, 5,6-DHT lesion, electrolytic lesions to dorsal and medial raphe nuclei showed no effect on WDS behavior, but L-5-hydroxytryptophan efficiently blocked it. Atropine and morphine considerably blocked KA-induced WDS behavior, but pilocarpine and nalorphine showed no effect. Bicuculline significantly enhanced, but aminooxyacetic acid blocked WDS. Intracerebroventricularly administered KA dose-dependently decreased the concentrations of noradrenaline and dopamine in the whole rat brain. The brain concentration of 5-hydroxytryptamine was unchanged. In contrast the concentration of 5-hydroxyindoleacetic acid increased. KA was ineffective regarding the GABA concentration and GAD activity. KA dose-dependently accelerated the disappearance of brain noradrenaline and dopamine after inhibition of catecholamine synthesis. KA, following inhibition of monoamine oxidase, increased the accumulation of 5-hydroxytryptamine, but failed to change the rate of decline of 5-hydroxyindoleacetic acid. KA failed to change the disappearance of brain 5-hydroxytryptamine after inhibition of its synthesis by PCPA. It is suggested that KA-induced WDS behavior is independent from the increased activity of serotonergic neurons in the central nervous system. KA-induced WDS appears to be under the inhibitory control of noradrenergic and GABA-ergic activity. The weaker inhibitory effect upon this behavior showed also dopaminergic and serotonergic neurons. The present experiments showed the close relationship between KA-induced WDS and shaking behavior in morphine abstinence, but basic differences in WDS behavior caused by excessive stimulation of serotonergic receptors.
CT Medical Descriptors:
*5,6 dihydroxytryptophan
*brain injury
*locus ceruleus
*raphe nucleus
*wet dog shakes

withdrawal syndrome
intracerebral drug administration
dose response
drug comparison
drug withdrawal
rat
drug response
therapy
central nervous system
animal experiment
intracerebroventricular drug administration
intraperitoneal drug administration
subcutaneous drug administration
Drug Descriptors:
*4 aminobutyric acid
*5 hydroxytryptophan
*oxidopamine
*aminoadipic acid
*apomorphine
*atropine
***benserazide**
*bis(4 methyl 1 homopiperazinylthiocarbonyl)disulfide
*aminooxyacetic acid
*clonidine
*cyproheptadine
*dopamine
*fenclonine
***glutamic acid diethyl ester**
*haloperidol
*kainic acid
***levodopa**
*metergoline
*metirosine
*morphine
*nalorphine
*neurotransmitter
*noradrenalin
*phentolamine
*pilocarpine
*serotonin
*yohimbine
bicuculline
propranolol

RN (4 aminobutyric acid) 28805-76-7, 56-12-2; (5 hydroxytryptophan) 4350-09-8, 56-69-9; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0; (aminoadipic acid) 52047-41-3; (apomorphine) 314-19-2, 58-00-4; (atropine) 51-55-8, 55-48-1; (benserazide) 14919-77-8, **322-35-0**; (bis(4 methyl 1 homopiperazinylthiocarbonyl)disulfide) 26087-98-9; (aminooxyacetic acid) 2921-14-4, 645-88-5; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (cyproheptadine) 129-03-3, 969-33-5; (dopamine) 51-61-6, 62-31-7; (fenclonine) 1991-78-2, 7424-00-2; (glutamic acid diethyl ester) 16450-41-2; (haloperidol) 52-86-8; (kainic acid) 487-79-6; (levodopa) **59-92-7**; (metergoline) 17692-51-2; (metirosine) 672-87-7; (morphine) 52-26-6, 57-27-2; (nalorphine) 1041-90-3, 57-29-4, 62-67-9; (noradrenalin) 1407-84-7, 51-41-2; (phentolamine) 50-60-2, 73-05-2; (pilocarpine) 148-72-1, 54-71-7, 92-13-7; (serotonin) 50-67-9; (yohimbine) 146-48-5, 65-19-0; (bicuculline) 485-49-4; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6

CN Fla 63; Ro 4 4602

CO Sigma (United States); Polfa (Poland); Sandoz (Luxembourg); Merck (Germany); Vacom (Yugoslavia); Koch light (United Kingdom); Ciba geigy (Switzerland); Chinoin (Hungary); Kistner (Sweden); Boehringer ingelheim (Germany); Richter (Hungary); Roche (Switzerland)

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L128 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:147868 BIOSIS
DN PREV200100147868
TI Atropisomeric **quinazolin**-4-one derivatives are potent noncompetitive alpha-**amino**-3-**hydroxy**-5-**methyl**-4-**isoxazolepropionic** acid (**AMPA**) receptor antagonists.
AU **Welch, W. M.**; Ewing, F. E.; Huang, J.; **Menniti, F. S.**; Pagnozzi, M. J.; Kelly, K.; Seymour, P. A.; Guanowsky, V.; Guhan, S.; Guinn, M. R.; Critchett, D.; Lazzaro, J.; Ganong, A. H.; DeVries, K. M.; Staigers, T. L.; **Chenard, B. L. (1)**
CS (1) Global Research and Development, Groton Laboratories, Pfizer Inc., Groton, CT, 06340: chenardbl@groton.pfizer.com USA
SO Bioorganic & Medicinal Chemistry Letters, (22 January, 2001) Vol. 11, No. 2, pp. 177-181. print.
ISSN: 0960-894X.
DT Article
LA English
SL English
AB Piriqualone (1) was found to be an antagonist of **AMPA** receptors. Structure-activity optimization was conducted on each of the three rings in 1 to afford a series of potent and selective antagonists. The sterically crowded environment surrounding the N-3 aryl group provided sufficient thermal stability for atropisomers to be isolated. Separation of these atropisomers resulted in the identification of (+)-38 (CP-465,022), a compound that binds to the **AMPA** receptor with high affinity (IC50=36nM) and displays potent anticonvulsant activity.
CC Pharmacology - Neuropharmacology *22024
Biochemical Studies - General *10060
Pathology, General and Miscellaneous - Therapy *12512
Pharmacology - General *22002
IT Major Concepts
Biochemistry and Molecular Biophysics; Pharmaceuticals (Pharmacology)
IT Chemicals & Biochemicals
CP-465,022: anticonvulsant - drug; alpha-**amino**-3-**hydroxy**-5-**methyl**-4-**isoxazolepropionic** acid receptor; piriqualone: alpha-**amino**-3-**hydroxy**-5-**methyl**-4-**isoxazolepropionic** acid receptor antagonist; **quinazolin**-4-one: alpha-**amino**-3-**hydroxy**-5-**methyl**-4-**isoxazolepropionic** acid receptor antagonist, derivatives
RN 199655-36-2 (CP-465,022)
1897-89-8 (PIRIQUALONE)
491-36-1 (**QUINAZOLIN**-4-ONE)

L128 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:45788 BIOSIS
DN PREV200100045788
TI **Quinazoline**-4-one **AMPA** antagonists.
AU **Chenard, Bertrand L.; Welch, Willard M. (1)**
CS (1) Mystic, CT USA
ASSIGNEE: Pfizer Inc

PI US 6060479 May 09, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents, (May 9, 2000) Vol. 1234, No. 2, pp. No Pagination. e-file. ISSN: 0098-1133.
DT Patent
LA English
AB The present invention relates to novel **quinazolin**-4-one derivatives of the formula I, as defined in the specification, pharmaceutical compositions containing such compounds the use of such compounds to treat neurodegenerative, psychotropic, and drug and alcohol induced central and peripheral nervous system disorders.
NCL 514258000
IT Major Concepts
Neurology (Human Medicine, Medical Sciences); Psychiatry (Human Medicine, Medical Sciences); Pharmaceuticals (Pharmacology)
IT Diseases
nervous system disorders: alcohol-induced, drug-induced, nervous system disease; neurodegenerative disorders: nervous system disease; psychotropic disorder: behavioral and mental disorders, nervous system disease
IT Chemicals & Biochemicals
quinazolin-4-one: **AMPA** antagonist, derivatives, pharmaceutical
RN 491-36-1 (**QUINAZOLIN**-4-ONE)

L128 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:355669 BIOSIS
DN PREV200000355669
TI Methaqualone derivatives are potent noncompetitive **AMPA** receptor antagonists.
AU **Chenard, B. L. (1)**; **Menniti, F. S.**; Pagnozzi, M. J.; Shenk, K. D.; Ewing, F. E.; **Welch, W. M.**
CS (1) Central Research Division, Pfizer Inc., Groton, CT, 06340 USA
SO Bioorganic & Medicinal Chemistry Letters, (5 June, 2000) Vol. 10, No. 11, pp. 1203-1205. print. ISSN: 0960-894X.
DT Article
LA English
SL English
AB **Quinazolin**-4-one derivatives of methaqualone substituted at C-2 define a new class of noncompetitive antagonists at **AMPA** receptors.
CC Biochemical Studies - General *10060
Pathology, General and Miscellaneous - Therapy *12512
Nervous System - Physiology and Biochemistry *20504
Pharmacology - General *22002
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination); Pharmacology
IT Parts, Structures, & Systems of Organisms
central nervous system: nervous system
IT Chemicals & Biochemicals
2-**amino**-3-(3-**hydroxy**-5-**methyl**-4-**isoxazolyl**)-**propionate** receptor; methaqualone derivative: anticonvulsant activity, noncompetitive 2-**amino**-3-(3-**hydroxy**-5-**methyl**-4-**isoxazolyl**)-**propionate** receptor antagonist, pyridine ring modification; **quinazolin**-4-one: synthesis
RN 491-36-1 (**QUINAZOLIN**-4-ONE)

L128 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:222771 BIOSIS
DN PREV200000222771
TI Discovery of a potent and selective series of noncompetitive **quinazolinone AMPA** antagonists.
AU **Welch, Willard M. (1)**; Huang, J. H. (1); Ewing, F. E. (1);

Menniti, F. S. (1); Pagnozzi, M. J. (1); Banker, M. J. (1); Devries, K. M. (1)
CS (1) Department of Medicinal Chemistry, Pfizer Inc, Eastern Point Road, Groton, CT, 06340 USA
SO Abstracts of Papers American Chemical Society, (2000) Vol. 219, No. 1-2, pp. MEDI 325.
Meeting Info.: 219th Meeting of the American Chemical Society. San Francisco, California, USA March 26-30, 2000 American Chemical Society . ISSN: 0065-7727.
DT Conference
LA English
SL English
CC Pharmacology - General *22002
Cytology and Cytochemistry - General *02502
Biochemical Methods - General *10050
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - General Metabolism; Metabolic Pathways *13002
Pathology, General and Miscellaneous - General *12502
Biochemical Studies - General *10060
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
IT Major Concepts
Pharmacology
IT Chemicals & Biochemicals
AMPA receptors [alpha-**amino**-3-**hydroxy**-5-**methyl-isoxazole propionate** receptors]; noncompetitive **quinazolinone AMPA** receptor antagonists: molecular properties, pharmaceuticals, pharmacodynamics, pharmacological properties, synthesis
IT Miscellaneous Descriptors
drug discovery; structure-activity relationships; Meeting Abstract

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L9 ANSWER 1 OF 4 CAPLUS COPYRIGHT 1999 ACS
PY 1999
1999
1999
1999
AN 1999:175749 CAPLUS
DN 130:218317
TI AMPA antagonists for the treatment of dyskinesias associated with dopamine agonist therapy
IN Chenard, Bertrand Leo; Menniti, Frank Samuel; Welch, Willard McKowan, Jr.
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K031-505
ICI A61K031-505, A61K031-195, A61K031-15
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 900568	A2	19990310	EP 1998-307181	19980904
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 11158072	A2	19990615	JP 1998-245269	19980831
	AU 9883120	A1	19990318	AU 1998-83120	19980904
	CA 2246839	AA	19990305	CA 1998-2246839	19980908
PRAI	US 1997-58098		19970905		

OS MARPAT 130:218317
AB The invention relates to a method of treating dyskinesias assocd. with dopamine agonist therapy in a mammal which comprises administering to said mammal a compd., as defined herein, which is an antagonist of the AMPA receptor. Dopamine agonist therapy, as referred to in the present invention, is generally used in the treatment of a central nervous system disorder such as Parkinson's disease. One example compd. of the 212 claimed was (S)-3-(2-chlorophenyl)-2-[2-(5-diethylaminomethyl-2-fluorophenyl)vinyl]-6-fluoro-3H-quinazolin-4-one.
ST AMPA antagonist dyskinesia dopamine agonist
IT Drug delivery systems
Parkinson's disease
(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)
IT AMPA receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)
IT Dyskinesia (nervous system)
(Parkinson's-assocd.; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)
IT 51-61-6, Dopamine, biological studies 59-92-7, biological studies
322-35-0, Benserazide 3257-47-4 28860-95-9, Carbidopa 199655-53-3
199655-54-4 199655-56-6 199655-57-7 199655-58-8 199655-59-9
199655-61-3 199655-62-4 199655-63-5 199655-64-6 199655-65-7
199655-66-8 199655-67-9 199655-68-0 199655-69-1 199655-70-4
199655-71-5 199655-72-6 199655-75-9 199655-76-0 199655-77-1
199655-78-2 199655-80-6 **199655-81-7** 199655-82-8

199655-84-0 199655-86-2 199655-87-3 199655-88-4 199655-89-5
199655-90-8 199655-91-9 199656-00-3 199656-44-5 212710-60-6
212710-61-7 212710-62-8 212710-64-0 212710-65-1 212710-66-2
212710-70-8 212765-03-2 212850-63-0 212850-64-1 212850-72-1
212850-74-3 212850-78-7 212850-79-8 212850-80-1 212850-81-2
212850-82-3 212916-59-1 212916-65-9 217821-32-4 217821-33-5
217821-34-6 217821-35-7 217821-36-8 217821-37-9 217821-38-0
217821-39-1 217821-41-5 217821-42-6 217942-51-3 217942-54-6
217942-55-7 217942-57-9 217942-58-0 217942-60-4 217942-62-6
217942-63-7 217942-64-8 217942-66-0 217942-68-2 217942-69-3
217942-71-7 217942-72-8 217942-74-0 217942-76-2 217942-78-4
217942-86-4 217942-87-5 221151-74-2 221151-75-3 221151-81-1
221151-83-3 221151-84-4 221151-88-8 221151-95-7 221152-14-3
221152-18-7 221152-21-2 221152-23-4 221152-26-7 221152-29-0
221152-30-3 221152-31-4 221152-32-5 221152-34-7 221152-35-8
221152-36-9 221152-37-0 221152-38-1 221152-39-2 221152-40-5
221152-41-6 221152-42-7 221152-43-8 221152-44-9 221152-45-0
221152-46-1 221152-47-2 221152-48-3 221152-49-4 221152-50-7
221152-51-8 221152-52-9 221152-53-0 221152-54-1 221152-55-2
221152-56-3 221152-57-4 221152-58-5 221152-59-6 221152-60-9
221152-61-0 221152-62-1 221152-63-2 221167-22-2 221167-24-4
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

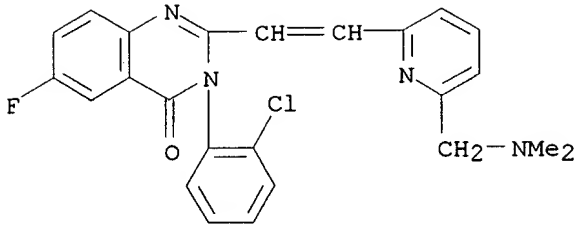
IT 77521-29-0, Ampa
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 9042-64-2, Dopa decarboxylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **199655-81-7**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

RN 199655-81-7 CAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)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L9 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1999 ACS
PY 1999
1999
1999
1999
AN 1999:175748 CAPLUS
DN 130:209717
TI Preparation of 3-(2-chlorophenyl)-2-[2-(6-diethylaminomethylpyridin-2-yl)vinyl]-6-fluoro-3H-quinazolin-4-one as an AMPA antagonist for the treatment of dyskinesias associated with dopamine agonist therapy.
IN Chenard, Bertrand Leo; Greenamyre, John Timothy; Menniti, Frank Samuel; Welch, Willard McKowan, Jr.
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K031-505
ICI A61K031-505, A61K031-195, A61K031-15
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 900567	A2	19990310	EP 1998-306661	19980820
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CA 2246560	AA	19990305	CA 1998-2246560	19980903
	JP 11139991	A2	19990525	JP 1998-249644	19980903
	AU 9883193	A1	19990318	AU 1998-83193	19980907
PRAI	US 1997-57965		19970905		

AB A method for the treatment of dyskinesias assocd. with dopamine agonist therapy comprising administration of an AMPA antagonist is claimed (no data). Thus, 3-(2-chlorophenyl)-6-fluoro-2-methyl-4-(3H)-quinazolinone (prepn. given) was refluxed with 2,6-pyridinedicarboxaldehyde, ZnCl2, and Ac2O in dioxane to give 33% 6-[2-[3-(2-chlorophenyl)-6-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl]vinyl]pyridine-2-carboxaldehyde. This was stirred with Et2NH and NaBH(AcO)3 in CH2Cl2 to give 24% title compd. as the monomaleate salt.
ST chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone prepn AMPA antagonist; quinazolinone chlorophenyldiethylaminomethylpyridinylvinyl prepn AMPA antagonist; dyskinesia treatment AMPA antagonist chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone
IT AMPA receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(antagonists; prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-one as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
IT Dyskinesia (nervous system)
(treatment; prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-one as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
IT **220931-86-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-

one as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **199655-81-7**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 59-92-7, L-Dopa, miscellaneous 322-35-0, Benserazide 28860-95-9, Carbidopa
RL: MSC (Miscellaneous)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 95-51-2, 2-Chloroaniline 109-89-7, reactions 320-98-9 5431-44-7, 2,6-Pyridinedicarboxaldehyde
RL: RCT (Reactant)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 38520-78-4P 49579-12-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **220931-86-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

RN 220931-86-2 CAPLUS
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

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CRN 199655-81-7
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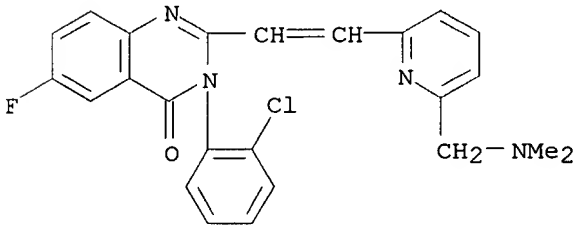
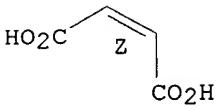


CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

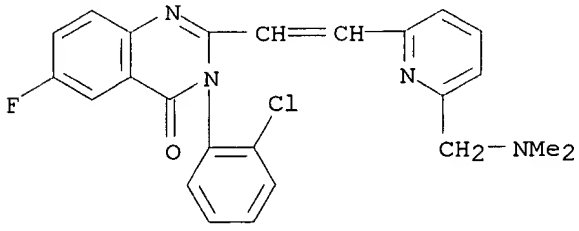
Double bond geometry as shown.



IT **199655-81-7**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

RN 199655-81-7 CAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



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PY   1998
     1998
AN   1998:608605  CAPLUS
DN   129:230733
TI   Preparation of atropisomers of 3-aryl-4(3H)-quinazolinones and their use
     as AMPA-receptor antagonists
IN   Welch, Willard McKowan, Jr.; Devries, Keith M.
PA   Pfizer Products Inc., USA
SO   PCT Int. Appl., 81 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  C07D239-91
     ICS  C07D401-06; C07D417-06; C07D401-14; C07D405-06; C07D413-06;
          A61K031-505; C07M007-00
CC   28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
     Section cross-reference(s): 1, 63
FAN.CNT 1
     PATENT NO.          KIND  DATE           APPLICATION NO.  DATE
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PI   WO 9838173          A1    19980903       WO 1998-IB150    19980206
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
           DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
           KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
           PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
           US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
           FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
           GA, GN, ML, MR, NE, SN, TD, TG
     AU 9856768          A1    19980918       AU 1998-56768    19980206
PRAI US 1997-38905       19970228
     WO 1998-IB150       19980206
OS   MARPAT 129:230733
GI
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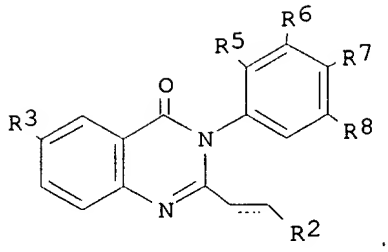

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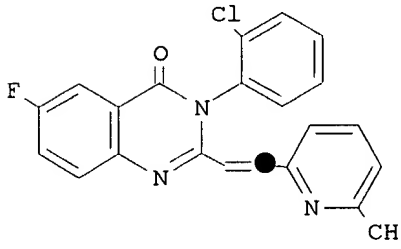

II

AB Title atropisomers [I; wherein R2 is an optionally substituted aryl or heteroaryl, R5 is alkyl, halo, CF3, alkoxy or alkylthio, R6, R7 and R8 are hydrogen or halo, and R3 is hydrogen, halo, CN, NO2, CF3, alkyl or alkoxy] are prepd. and are useful as AMPA receptor antagonists, particularly in the treatment of neurodegenerative and CNS-trauma related conditions (no data). The title (S)-atropisomer II was prepd. from 2-chloroaniline, 6-fluoro-2-methylquinoxalin-4-one which was prepd. from hydrogenation, acetylation, and cyclization of 2-nitro-5-fluorobenzoic acid, followed by reaction with 2,6-pyridinedicarboxaldehyde, and diethylamine, and was column sepd.

ST quinazolinone prepn; atropisomer quinazolinone sepn HPLC receptor antagonist

IT Separation
(HPLC column; prepn. and sepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT AMPA receptors
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antagonists; prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT 212850-63-0P 212850-64-1P 212850-65-2P 212850-66-3P 212850-68-5P
212850-70-9P 212850-72-1P 212850-73-2P 212850-74-3P 212850-75-4P
212850-76-5P 212850-77-6P 212850-78-7P 212850-79-8P 212850-80-1P
212850-81-2P 212850-82-3P 212916-59-1P 212916-60-4P 212916-61-5P
212916-62-6P 212916-63-7P 212916-64-8P 212916-65-9P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT 10200-43-8P 49579-12-6P 68683-04-5P 78441-69-7P 82586-66-1P
113732-84-6P 141567-53-5P 174608-36-7P 194473-04-6P 199599-68-3P
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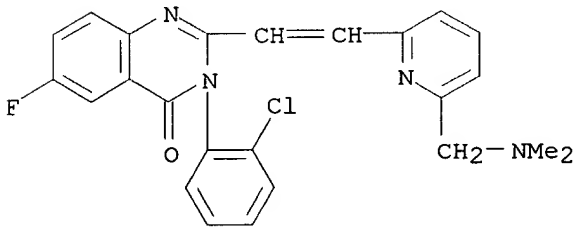
212765-26-9P 212765-27-0P 212765-28-1P 212772-14-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT **199655-81-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

RN 199655-81-7 CAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



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L9 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS
PY 1997
1997
1997
1999
1999
1999
AN 1997:752948 CAPLUS
DN 128:34774
TI Preparation of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists.
IN Elliott, Mark Leonard; Welch, Willard Mckowan Jr
PA Pfizer Inc., USA; Elliott, Mark Leonard; Welch, Willard Mckowan Jr.
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D401-06
ICS C07D401-04; C07D401-14; C07D405-06; C07D403-06; C07D239-91; C07D417-14; C07D417-06; A61K031-505
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9743276	A1	19971120	WO 1997-IB134	19970217
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2252907	AA	19971120	CA 1997-2252907	19970217
	AU 9715549	A1	19971205	AU 1997-15549	19970217
	EP 901487	A1	19990317	EP 1997-901749	19970217
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	CN 1218464	A	19990602	CN 1997-194654	19970217
	NO 9805293	A	19990113	NO 1998-5293	19981113

PRAI US 1996-17738 19960515
WO 1997-IB134 19970217
OS MARPAT 128:34774
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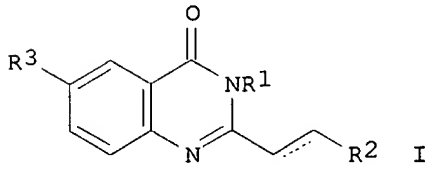

I

AB Title compds. [I; R1 = (substituted) Ph, pyridyl; R2 = (substituted) Ph, 5-6 membered heterocyclyl; R3 = H, halo, cyano, No2, CF3, alkyl, alkoxy], were prepd. Thus, 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylvinyl)-3H-quinazolin-4-one was hydrogenated in EtOAc over Pd/C to give 100% 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylethyl)-3H-quinazolin-4-one. Tested I inhibited AMPA receptor activation-induced 45Ca2+ uptake with IC50 <5 .mu.M.

ST quinazolinone prepn AMPA receptor antagonist; nervous system agents quinazolinone

IT Nervous system agents
Neurotransmitter antagonists
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

IT 3257-47-4P 199655-35-1P 199655-36-2P 199655-37-3P 199655-38-4P
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RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

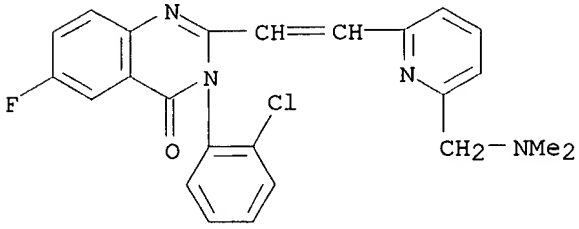
IT 95-51-2, 2-Chloroaniline 320-98-9 340-57-8 5431-44-7, 2,6-Pyridinedicarboxaldehyde 20949-84-2, 2-Methylthiazole-4-carboxaldehyde 49579-01-3 49579-08-0 199599-68-3 199656-42-3 199656-43-4
RL: RCT (Reactant)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

IT 38520-78-4P 49579-12-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

IT **199655-81-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

RN 199655-81-7 CAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> d std bib ab clm

L14 ANSWER 1 OF 1 USPATFULL
AN 97:86624 USPATFULL
TI Excitatory amino acid receptor antagonists
IN Arnold, M. Brian, Franklin, IN, United States
Augenstein, Nancy K., Indianapolis, IN, United States
Lunn, William H. W., Indianapolis, IN, United States
Ornstein, Paul L., Indianapolis, IN, United States
Schoepp, Darryle D., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5670516 19970923
AI US 1995-456439 19950601 (8)
RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994, now abandoned which is a division of Ser. No. US 1993-111747, filed on 25 Aug 1993, now patented, Pat. No. US 5399696 which is a division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957
DT Utility
LN.CNT 3909
INCL INCLM: 514/307.000
INCLS: 546/147.000
NCL NCLM: 514/307.000
NCLS: 546/147.000
IC [6]
ICM: C07D215-14
ICS: A61K031-47
EXF 546/23; 546/146; 546/147; 546/148; 546/150; 514/307
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 97:86624 USPATFULL
TI Excitatory amino acid receptor antagonists
IN Arnold, M. Brian, Franklin, IN, United States
Augenstein, Nancy K., Indianapolis, IN, United States
Lunn, William H. W., Indianapolis, IN, United States
Ornstein, Paul L., Indianapolis, IN, United States
Schoepp, Darryle D., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5670516 19970923
AI US 1995-456439 19950601 (8)
RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994, now abandoned which is a division of Ser. No. US 1993-111747, filed on 25 Aug 1993, now patented, Pat. No. US 5399696 which is a division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957
DT Utility
EXNAM Primary Examiner: Davis, Zinna Northington
LREP Hay, Martin A.; Leeds, James P.
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3909
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders. This invention also provides synthetic methods for preparing decahydroisoquinolines, as well as, novel intermediates in the synthesis thereof.
CLM What is claimed is:
1. A compound of the formula ##STR87## wherein: R.sup.1 is hydrogen,

C.sub.1 -C.sub.10 alkyl, arylalkyl, alkoxycarbonyl or acyl; R.sup.2 is hydrogen, C.sub.1 -C.sub.6 alkyl, substituted alkyl, cycloalkyl, or arylalkyl; R.sup.3 is CO.sub.2 H, SO.sub.3 H, CONHSO.sub.2 R.sup.8, or a group of formula ##STR88## W is (CH.sub.2).sub.n, S, SO, SO.sub.2 ; Y is CHR.sup.7, NR.sup.4, O, S, SO, or SO.sub.2 ; Z is NR.sup.6, CHR.sup.7, or CH; or W and Y together are HC.dbd.CH or C.tbd.C, or Y and Z together are HC.dbd.CH or C.tbd.C; R.sup.4 is hydrogen, C.sub.1 -C.sub.4 alkyl, phenyl, or acyl; R.sup.5 is hydrogen, C.sub.1 -C.sub.4 alkyl, CF.sub.3, phenyl, hydroxy, amino, bromo, iodo, or chloro; R.sup.6 is acyl; R.sup.7 is independently hydrogen, C.sub.1 -C.sub.4 alkyl, phenyl, or substituted phenyl; R.sup.8 is C.sub.1 -C.sub.4 alkyl or tetrazole-5-yl; and n is 0, 1, or 2; provided that when Y is NR.sup.4, O, S, SO, or SO.sub.2, W is (CH.sub.2).sub.n and Z is CHR.sup.7 or CH; further provided that when W is S, SO, or SO.sub.2, Y is CHR.sup.7, Z is CHR.sup.7 or CH, or Y and Z together are HC.dbd.CH or C.tbd.C; further provided that when W and Z are CH.sub.2, Y is not S; further provided that when W and Y together are HC.dbd.CH or C.tbd.C, Z is CHR.sub.7 ; or a pharmaceutically acceptable salt thereof.

2. A compound of claim 1 wherein: R.sup.1 is hydrogen or alkoxycarbonyl; R.sup.2 is hydrogen or C.sub.1 -C.sub.6 alkyl; R.sup.3 is a group selected from the group consisting of CO.sub.2 H, SO.sub.3 H, CONHSO.sub.2 R.sup.8, and ##STR89## W is S or (CH.sub.2).sub.n ; n is 0, 1, or 2; Y is CHR.sup.7, S, SO.sub.2 or O; Z is CHR.sup.7 or NR.sup.6 ; or Y and Z together are HC.dbd.CH; R.sup.6 is formyl; R.sup.7 is independently hydrogen, C.sub.1 -C.sub.4 alkyl, or phenyl; R.sup.8 is C.sub.1 -C.sub.4 alkyl or tetrazole-5-yl; or a pharmaceutically acceptable salt thereof.

3. A compound of claim 2 wherein R.sup.1 and R.sup.2 are hydrogen, or a pharmaceutically acceptable salt thereof.

4. A compound of claim 2 wherein: R.sup.1 is hydrogen or alkoxycarbonyl; R.sup.2 is hydrogen or C.sub.1 -C.sub.6 alkyl; R.sup.3 is a group selected from the group consisting of SO.sub.3 H and a group of the formula ##STR90## W is S, SO.sub.2 or (CH.sub.2).sub.n ; n is 0, 1, or 2; Y is CHR.sup.7, S, or SO.sub.2 ; Z is CHR.sup.7 ; R.sup.5 is hydrogen, C.sub.1 -C.sub.4 alkyl, or CF.sub.3 ; and R.sup.7 is hydrogen, C.sub.1 -C.sub.4 alkyl, or phenyl; or a pharmaceutically acceptable salt thereof.

5. A compound of claim 4 wherein: R.sup.1 and R.sup.2 are hydrogen, or a pharmaceutically acceptable salt thereof.

6. A compound of claim 4 wherein: R.sup.1 and R.sup.2 are hydrogen; R.sup.3 is a group selected from the group of the formula ##STR91## W is (CH.sub.2).sub.n ; n is 0; Y is CHR.sup.7, S, or SO.sub.2 ; Z is CHR.sup.7 ; R.sup.5 is hydrogen or C.sub.1 -C.sub.4 alkyl; and R.sup.7 is hydrogen, C.sub.1 -C.sub.4 alkyl, or phenyl; or a pharmaceutically acceptable salt thereof.

7. A compound of claim 6 wherein R.sup.3 is a group of the formula ##STR92## or a pharmaceutically acceptable salt thereof.

8. A compound of claim 6 wherein R.sup.3 is a group of the formula ##STR93## or a pharmaceutically acceptable salt thereof.

9. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

10. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

11. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)-2-thiaethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

12. The compound of claim 6 which is (3S,4aR,6S,8aR)-6-[2-(1(2)H-tetrazole-5-yl)-2-thiaethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

13. The compound of claim 6 which is 6-[2-(3-hydroxyisoxazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

14. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(3-hydroxyisoxazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

15. The compound of claim 6 which is 6-[(1(2-4)H-1,2,4-triazole-5-yl)sulfonylmethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

16. The compound of claim 6 which is (3S,4aR,6S,8aR)-6-[(1(2-4)H-1,2,4-triazole-5-yl)sulfonylmethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

17. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)-1-methylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

18. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(1(2)H-tetrazole-5-yl)-1-methylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

19. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)-1-phenylethyl]-decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

20. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(1(2)H-tetrazole-5-yl)-1-phenylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

21. A method of blocking the **AMPA** excitatory amino acid receptor in mammals which comprises administering to a mammal requiring decreased excitatory amino acid neurotransmission a pharmaceutically-effective amount of a compound of claim 1.

22. A method of blocking the **AMPA** excitatory amino acid receptor in mammals which comprises administering to a mammal requiring decreased excitatory amino acid neurotransmission a pharmaceutically-effective amount of a compound of claim 6.

23. A method of treating a neurological disorder in a patient, which comprises administering to a patient in need thereof, an effective amount of a compound of claim 1.

24. The method of claim 23 wherein said neurological disorder is

cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**.

25. The method of claim 23 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, cardiac arrest, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, chronic pain, psychosis, emesis, muscular spasms, amyotrophic lateral sclerosis, or ocular damage and retinopathy.

26. The method of claim 23 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, ocular damage and retinopathy, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, or chronic pain.

27. The method of claim 23 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, or ocular damage and retinopathy.

28. A method of treating a neurological disorder in a patient, which comprises administering to a patient in need thereof, an effective amount of a compound of claim 6.

29. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerbral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**.

30. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, cardiac arrest, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, chronic pain, psychosis, emesis, muscular spasms, amyotrophic lateral sclerosis, or ocular damage and retinopathy.

31. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, ocular damage and retinopathy, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, or chronic pain.

32. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, or ocular damage and retinopathy.

33. A method of producing analgesia in mammals which comprises administering to a mammal an effective amount of a compound of claim 1.

34. A method of producing analgesia in mammals which comprises administering to a mammal an effective amount of a compound of claim 6.

35. A pharmaceutical formulation comprising a compound of claim 1 and a pharmaceutically-acceptable carrier, diluent, or excipient.

36. A pharmaceutical formulation comprising a compound of claim 6 and a pharmaceutically-acceptable carrier, diluent, or excipient.

37. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

38. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)-2-thiaethyl]-decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt.

39. A formulation according to claim 36 wherein the compound is 6-[2-(3-hydroxyisoxazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

40. A formulation according to claim 35 wherein the compound is 6-[(1(2-4)H-1,2,4-triazole-5-yl)sulfonylmethyl]-decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

41. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)-1-methylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

42. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)-1-phenylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

=> d l34 std bib ab hit

L34 ANSWER 1 OF 5 USPATFULL
AN 97:16213 USPATFULL
TI Isoquinolinyl-carboxylic acid receptor antagonists compounds
IN Huff, Bret, Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5606062 19970225 <--
AI US 1995-457556 19950601 (8)
RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994 which is a division of Ser. No. US 1993-111747, filed on 25 Aug 1993, now patented, Pat. No. US 5399696 which is a division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957
DT Utility
LN.CNT 3730
INCL INCLM: 546/147.000
NCL NCLM: 546/147.000
IC [6]
ICM: C07D217-16
EXF 546/146; 546/147
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 97:16213 USPATFULL
TI Isoquinolinyl-carboxylic acid receptor antagonists compounds
IN Huff, Bret, Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5606062 19970225 <--
AI US 1995-457556 19950601 (8)
RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994 which is a division of Ser. No. US 1993-111747, filed on 25 Aug 1993, now patented, Pat. No. US 5399696 which is a division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957
DT Utility
EXNAM Primary Examiner: Davis, Zinna Northington
LREP Hay, Martin A.; Leeds, James P.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3730
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders. This invention also provides synthetic methods for preparing decahydroisoquinolines, as well as, novel intermediates in the synthesis thereof.
PI US 5606062 19970225 <--
SUMM Excitatory amino acid excitotoxicity has been implicated in the pathophysiology of a number of neurological disorders. This excitotoxicity has been implicated in the pathophysiology of acute and chronic neurodegenerative conditions including cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, perinatal hypoxia, cardiac arrest, hypoglyemic neuronal damage, ocular damage and retinopathy, and idiopathic and drug-induced Parkinson's Disease. Other neurological conditions, that are caused by glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary

incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive **dyskinesia**. The use of a neuroprotective agent, such as an AMPA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The EAA antagonists are also useful as analgesic agents.

SUMM Further embodiments of the invention include a method of blocking the AMPA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to the excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.

SUMM The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

=> d l34 std bib ab hit 2

L34 ANSWER 2 OF 5 USPATFULL
AN 96:53325 USPATFULL
TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists
IN Ornstein, Paul L., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5527810 19960618 <--
AI US 1994-255590 19940608 (8)
RLI Division of Ser. No. US 1992-972679, filed on 6 Nov 1992, now patented, Pat. No. US 5356902
DT Utility
LN.CNT 1477
INCL INCLM: 514/307.000
INCLS: 546/144.000; 546/147.000
NCL NCLM: 514/307.000
NCLS: 546/144.000; 546/147.000
IC [6]
ICM: A01N043-42
ICS: C07D217-00
EXF 546/144; 546/147; 514/307
AN 96:53325 USPATFULL
TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists
IN Ornstein, Paul L., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5527810 19960618 <--
AI US 1994-255590 19940608 (8)
RLI Division of Ser. No. US 1992-972679, filed on 6 Nov 1992, now patented, Pat. No. US 5356902
DT Utility
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Covington, Raymond
LREP Hay, Martin A.; Leeds, James P.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1477
AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders. This invention also provides synthetic methods for preparing decahydroisoquinolines.
PI US 5527810 19960618 <--
SUMM Excitatory amino acid excitotoxicity has been implicated in the pathophysiology of a number of neurological disorders. This excitotoxicity has been implicated in the pathophysiology of acute and chronic neurodegenerative conditions including cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, ocular damage and retinopathy, and idiopathic and drug-induced Parkinson's Disease. Other neurological conditions, that are caused by glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive

dyskinesia. The use of a neuroprotective agent, such as an AMPA or NMDA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The excitatory amino acid antagonists are also useful as analgesic agents.

SUMM Further embodiments of the invention include a method of blocking the AMPA or the NMDA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to these excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.

SUMM The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

CLM What is claimed is:

2. The method of claim 1 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**.

7. The method of claim 6 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerbral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**.

=> d l34 std bib ab hit 3

L34 ANSWER 3 OF 5 USPATFULL
AN 95:78190 USPATFULL
TI Aryl-spaced decahydroisoquinoline-3-carboxylic acids as excitatory amino acid receptor antagonists
IN Ornstein, Paul L., Carmel, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5446051 19950829 <--
AI US 1994-251809 19940531 (8)
DT Utility
LN.CNT 1093
INCL INCLM: 514/307.000
INCLS: 546/022.000; 546/147.000
NCL NCLM: 514/307.000
NCLS: 546/022.000; 546/147.000
IC [6]
ICM: C07D217-06
ICS: A61K031-47
EXF 546/22; 546/146; 546/147; 514/307
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 95:78190 USPATFULL
TI Aryl-spaced decahydroisoquinoline-3-carboxylic acids as excitatory amino acid receptor antagonists
IN Ornstein, Paul L., Carmel, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5446051 19950829 <--
AI US 1994-251809 19940531 (8)
DT Utility
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Davis, Zinna N.
LREP Hay, Martin A.; Dodd, Thomas J.; Boone, David E.
CLMN Number of Claims: 40
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1093
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides novel decahydroisoquinoline derivatives which are useful as excitatory amino acid antagonists. The invention also provides for methods of using these derivatives to treat various neurological disorders.
PI US 5446051 19950829 <--
SUMM Use of Formula (I) compounds as AMPA selective antagonists is seen as potentially beneficial in treating a number of neurodegenerative conditions including, but not limited to Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, cognitive disorders, Parkinson's Disease, anxiety, emesis, brain edema, chronic pain and tardive **dyskinesia**, among others. Formula (I) compounds are also contemplated for use to abate cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, and spinal cord and brain trauma injuries. Further, Formula (I) compounds are contemplated for use as analgesic agents.

SUMM The formula I compounds of the present invention are also believed to

have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, drug tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

=> d l34 std bib ab hit 4

L34 ANSWER 4 OF 5 USPATFULL
AN 95:25041 USPATFULL
TI Isoquinolinyl compounds which are intermediates
IN Arnold, M. Brian, Franklin, IN, United States
Augenstein, Nancy K., Indianapolis, IN, United States
Lunn, William H. W., Indianapolis, IN, United States
Ornstein, Paul L., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5399696 19950321 <--
AI US 1993-111747 19930825 (8)
RLI Division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957
DT Utility
LN.CNT 3727
INCL INCLM: 546/147.000
NCL NCLM: 546/147.000
IC [6]
ICM: C07D217-02
EXF 546/147; 546/15
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 95:25041 USPATFULL
TI Isoquinolinyl compounds which are intermediates
IN Arnold, M. Brian, Franklin, IN, United States
Augenstein, Nancy K., Indianapolis, IN, United States
Lunn, William H. W., Indianapolis, IN, United States
Ornstein, Paul L., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5399696 19950321 <--
AI US 1993-111747 19930825 (8)
RLI Division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957
DT Utility
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Davis, Zinna N.
LREP Leeds, James P.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3727
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders. This invention also provides synthetic methods for preparing decahydroisoquinolines, as well as, novel intermediates in the synthesis thereof.
PI US 5399696 19950321 <--
SUMM Excitatory amino acid excitotoxicity has been implicated in the pathophysiology of a number of neurological disorders. This excitotoxicity has been implicated in the pathophysiology of acute and chronic neurodegenerative conditions including cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, perinatal hypoxia, cardiac arrest, hypoglyemic neuronal damage, ocular damage and retinopathy, and idiopathic and drug-induced Parkinson's Disease. Other neurological conditions, that are caused by

glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive **dyskinesia**. The use of a neuroprotective agent, such as an AMPA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The EAA antagonists are also useful as analgesic agents.

SUMM Further embodiments of the invention include a method of blocking the AMPA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to the excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.

SUMM The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

=> d 134 std bib ab hit 5

L34 ANSWER 5 OF 5 USPATFULL
AN 94:91059 USPATFULL
TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists
IN Ornstein, Paul L., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5356902 19941018 <--
AI US 1992-972679 19921106 (7)
DT Utility
LN.CNT 1383
INCL INCLM: 514/307.000
INCLS: 546/144.000; 546/147.000
NCL NCLM: 514/307.000
NCLS: 546/144.000; 546/147.000
IC [5]
ICM: A01N043-42
ICS: C07D217-00
EXF 546/147; 546/144; 514/307
AN 94:91059 USPATFULL
TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists
IN Ornstein, Paul L., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5356902 19941018 <--
AI US 1992-972679 19921106 (7)
DT Utility
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Covington, Raymond
LREP Leeds, James P.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1383
AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders.
PI US 5356902 19941018 <--
SUMM Excitatory amino acid excitotoxicity has been implicated in the pathophysiology of a number of neurological disorders. This excitotoxicity has been implicated in the pathophysiology of a cute and chronic neurodegenerative conditions including cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, ocular damage and retinopathy, and idiopathic and drug-induced Parkinson's Disease. Other neurological conditions, that are caused by glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive **dyskinesia**. The use of a neuroprotective agent, such as an AMPA or NMDA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The excitatory amino acid antagonists are also useful as analgesic agents.

SUMM Further embodiments of the invention include a method of blocking the AMPA or the NMDA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to these excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.

DETD The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

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L11 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS
PY 1996
1996
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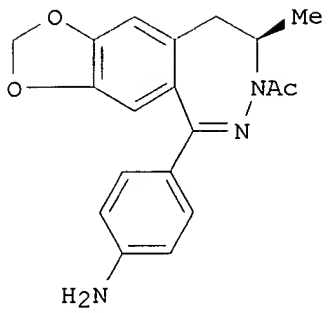
AN 1996:307308 CAPLUS
DN 124:343338
TI Physical form of dihydro-2,3-benzodiazepine derivative useful as an **AMPA antagonist**
IN Anderson, Benjamin Alan; Hansen, Marvin Martin; Vicenzi, Jeffrey Thomas; Varie, David Lee; Zmijewski, Milton Joseph, Jr.; Harkness, Allen Robert
PA Lilly, Eli, and Co., USA
SO Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07D491-056
ICS A61K031-55
ICI C07D491-056, C07D317-00, C07D243-00
CC 28-21 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 16, 63
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 699676	A1	19960306	EP 1995-306048	19950830
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, MC, NL, PT, SE				
	NO 9503395	A	19960301	NO 1995-3395	19950830
	CA 2157247	AA	19960301	CA 1995-2157247	19950830
	FI 9504065	A	19960301	FI 1995-4065	19950830
	AU 9530356	A1	19960314	AU 1995-30356	19950830
	AU 696243	B2	19980903		
	JP 08092255	A2	19960409	JP 1995-221572	19950830
	CN 1122338	A	19960515	CN 1995-109526	19950830
	HU 72673	A2	19960528	HU 1995-2547	19950830
	BR 9503844	A	19960910	BR 1995-3844	19950830
	IL 115101	A1	19981227	IL 1995-115101	19950830
PRAI	US 1994-298645	19940831			
	US 1995-413024	19950328			
	US 1994-289645	19940831			

OS CASREACT 124:343338
GI



I

AB A phys. form of (R)-7-acetyl-5-(4-aminophenyl)-8,9-dihydro-8-methyl-7H-1,3-dioxolo[4,5-h][2,3]benzodiazepine (I) is disclosed, having an x-ray powder diffraction pattern with d spacings at 10.61, 8.83, 6,78, 5.83, 4.13 and 3.74 .ANG.. The compd. is an **AMPA antagonist** (no data), useful for treating a variety of CNS and other disorders. I is prepd. in approx. 7 steps with several variations. For example, reductive fermn. of (3,4-methylenedioxyphenyl)acetone with Zygosaccharomyces rouxii ATCC 14462 gave (S)-.alpha.-methyl-1,3-benzodioxole-5-ethanol in 85-90% isolated yield and 100% ee. This underwent cyclization with p-nitrobenzaldehyde to a benzopyran deriv. (87-93%), atm. hydroxylation in DMSO-DMF to a cyclic hemiacetal, ring cleavage by AcNHNH2 to an alc./hydrazone (91%), mesylation of the alc. (87%), cyclization of the mesylate/hydrazone (90%), and redn. of the nitro group with aq. K formate over Pd/C (93%), giving form IV of I. Two chem. variants of the 1st step, and prepns. of forms I, II, and III of I using different redn. procedures in the last step, are also described.

ST benzodiazepine prepn **AMPA antagonist**; dioxolobenzodiazepine acetylaminophenyldihydromethyl form IV prepn

IT Analgesics
Anticonvulsants and Antiepileptics
Antiemetics
Anxiolytics
Muscle relaxants
Nervous system agents
(prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Saccharomyces rouxii
(reductive fermn. of (methylenedioxyphenyl)acetone; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Drug dependence
Parkinsonism
(treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Mental disorder
(Alzheimer's disease, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Tranquilizers and Neuroleptics
(antipsychotics, prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Mental disorder
(dementia, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Nervous system
(disease, Huntington's chorea, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor

antagonist)

IT Nervous system
(disease, amyotrophic lateral sclerosis, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Bladder
(disease, incontinence, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Nervous system
(disease, tardive **dyskinesia**, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Brain, disease
(edema, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Neurotransmitter antagonists
(glutamatergic, prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(glutamatergic, AMPA-binding, prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Eye, disease
(injury, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Brain, disease
(ischemia, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Headache
(migraine, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Eye, disease
(retinopathy, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT Brain, disease
(stroke, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT 172542-26-6P, (S)-.alpha.-Methyl-1,3-benzodioxole-5-ethanol
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(intermediate; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT 161832-64-0P 172542-27-7P 172542-28-8P 172542-29-9P 172542-30-2P
172542-31-3P 172721-25-4P 172721-26-5P 172721-27-6P 176777-96-1P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT 161832-65-1P
RL: BAC (Biological activity or effector, except adverse); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)

IT 124-63-0, Methanesulfonyl chloride 555-16-8, p-Nitrobenzaldehyde, reactions 1068-57-1, Acetic hydrazide 2635-13-4, 4-Bromo-1,2-methylenedioxybenzene 4676-39-5, (3,4-Methylenedioxyphenyl)acetone 16088-62-3, (S)-(-)-Propylene oxide, reactions

RL: RCT (Reactant)
(starting material; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor **antagonist**)